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ERYTHEMA ELEVATUM DIUTINUM.

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At the turn of the century reports appeared in the dermatological literature dealing with a group of dermatoses of an erythematous character which were distinguished from the well known erythemas by their tendency to persist and by the fibrotic transformation of some of their individual lesions. Rheumatism or gout were considered to be responsible. Another group of dermatoses, resembling the first in their erythemato-fibrotic morphology, showed in addition a tendency to a ringed or circular arrangement of their individual lesions. Both groups had in common localization on the extremities, and sometimes also on the face. Owing to the superficial morphological resemblance of the two groups, and also to the fact that the histology of the conditions at the time was not well understood, confusion arose as to the classification of these cases, and for a considerable time they were regarded either as identical, or at least as different stages of the same pathological process.

Hutchinson (1878) described the case of a man of 58 who had large persistent patches on the legs, the backs of the hands, the fingers and one forearm. These patches at first consisted of distinct tubercles, which afterwards became confluent and then "lost their tubercular character". The patches were of purple tint, raised above the surface, the margins for the most part irregular and abruptly defined. The surface was smooth or sometimes covered with dry scales. The elevation was mainly due to oedema, as the thickening dissipated to a great extent on pressure. The patient was gouty and died five years later of kidney and bladder disease (Fig. 1).

In a later paper (1888–89) Hutchinson mentions three more cases. The first two were physicians, one aged 70 years and probably gouty ; the other aged 40 years with no history of gout. The older one presented lesions on the toes which disappeared after 1 year, while the second had one hand affected and the condition persisted for many months. In both cases the patches were thickened with abrupt edges in some parts and of a dusky purple tint. Chil-

Fig. 1.

blains could be excluded, and Hutchinson concluded that the condition in both patients was due to " a state of permanent weakening and dilatation of veins ".

The other case concerned a man aged 65 years. The skin was in a state of senile atrophy. The lesions involved the hands, the whole of the front of his ankles, the dorsal surface of his feet, elbows, front of the wrists and the parts in front and behind the knees. The patches were dusky in colour, considerably thickened and hard to the touch. The boundaries of the indurated patches were ill defined, and a curious feature was the presence of little cords,

like hardened lymphatics or small veins, running upwards from the diseased parts. The patient believed that his condition was induced by injury 10 years previously. Hutchinson himself was reluctant to give the condition a name or to express an opinion as to the nature of the malady, but he regarded all the cases as probably belonging to the same group of diseases.

In 1889 Bury published " a case of erythema with remarkable nodular thickening and induration of skin, associated with intermittent albuminuria ".

She was a 12-year-old girl, the family history being irrelevant, who had had measles when five, and scarlet fever when nine years of age followed by

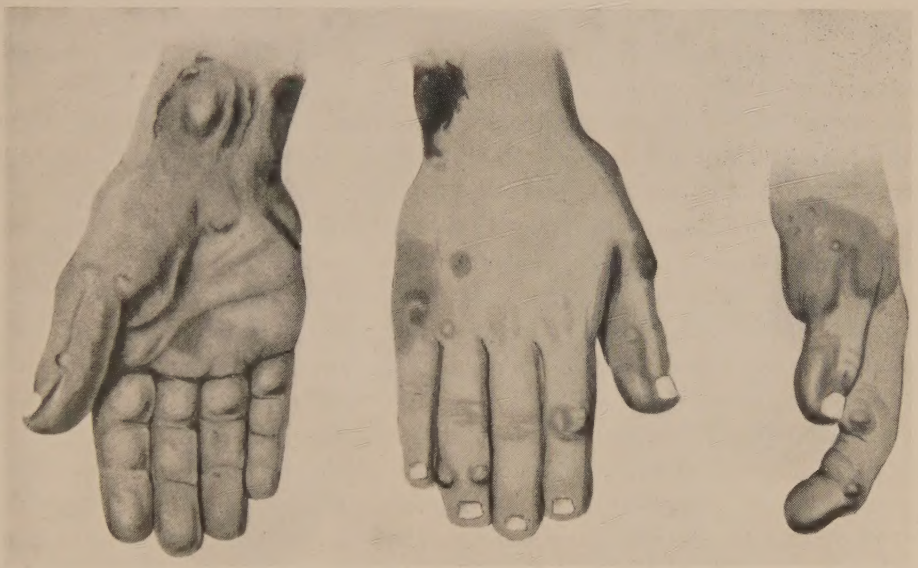

Fig. 2.

rheumatic fever. She presented a peculiar erythematous eruption of the hands, the distribution and general characters of which are shown in Fig. 2. The eruption began on the toes, then attacked the knees, the elbows, and lastly the fingers. She complained of much itching and tingling of the hands, especially at night when " she got properly warm in the house ". The hands were swollen and there was much thickening of the superficial tissues on the palmar aspect, where the skin had a peculiar purple tint. The purplish thickenings had well-defined raised edges, especially marked along the radial side of the thumb, and at this time the thickened edge was nodular ; but the distinct lumps, on the backs of the fingers indicated in the drawing, were features of a later stage. The nodules were as firm as leather or hard as cartilage. They did not show any tendency to soften. There were also raised patches of erythema on the backs of the elbows and to a less extent over the knees. The

colour was that of a bright erythema, which faded to leave a yellowish tint. The toes were slightly livid and swollen. The trunk and other parts of the body were free from the eruption. The affected parts felt warmer, but were not tender to touch. The eruption faded during the last three months, whereas the nodules increased in size. The patient also suffered from intermittent albuminuria.

Hutchinson, seeing the picture of Bury's case, thought it closely resembled his own original case ; three years later that patient was still in the same condition (Hutchinson, 1892).

In 1890 Hutchinson mentioned two other cases which he considered to be examples of the same malady in its earliest form. One was a man of 65 who was accustomed to ride much on a horseback. He was gouty. He developed the eruption on the inner side of the left knee, where it grips the saddle. The patch was raised, at least a quarter of an inch thick and as large as the palm of the hand. The second case was a man of 56, gouty and with a family history of gout. This patient developed a large dusky purple patch on the forehead and two little patches on the wrists. Hutchinson (1894) regarded these cases as starting from local injury and spreading as an infection.

Radcliffe-Crocker and Williams (1894*a*) described a case of a 6-year-old girl with a strong history of gout and rheumatism on mother's side, who, 5 months before attending the hospital, developed lesions on the knees followed by others on the buttocks, elbows and then on the hands. The lesion was " raised one eighth of an inch, convex, sharply defined, pale purplish in colour, with a few dilated vessels over it, sometimes whiter on pressure, but diminishing very little in size ; firm to the touch, very tender, but not painful except when pressed upon. It did not itch or burn. When regressing the lesions produced a wrinkling of the skin at their borders, later a purple tint which faded to leave a brownish discoloration. The lesions on the backs of the hands were distinctly nodular, on the palmar surface more diffused from coalescence of the component nodules. The affected parts were hotter to the touch, the surface smooth or slightly scaly " (Fig. 3).

The case was shown to the Dermatological Society for diagnosis and Hutchinson suggested that it resembled the case published by Bury.

Subsequently, Radcliffe-Crocker and Williams (1894*b*), reviewing all known cases and being fully aware that the small number of cases so far known did not lend itself to the description of a complete symptomatology, suggested a purely descriptive term for the whole group : erythema elevatum diutinum. They intended to indicate that the group was characterized by erythematous, raised, persistent lesions. They were convinced of the similarity of their own and Bury's cases, but thought the differences between these and those of Hutchinson were considerable. This made them distinguish two types but they suggested that perhaps they might merely be two phases of the same

process. They distinguished, therefore, a Bury type and a Hutchinson type of erythema elevatum diutinum. The Bury type occurred in young females, with a personal or family history of gout or rheumatism, who showed over the joints and on the palms, erythematous nodules becoming confluent and purplish, which may or may not persist, never spreading over large areas, getting paler but being firm on pressure. The Hutchinson type occurred entirely in elderly gouty males. The lesions were flattish nodules over bony surfaces, of purplish colour, persisting throughout life, spreading widely and of an oedematous

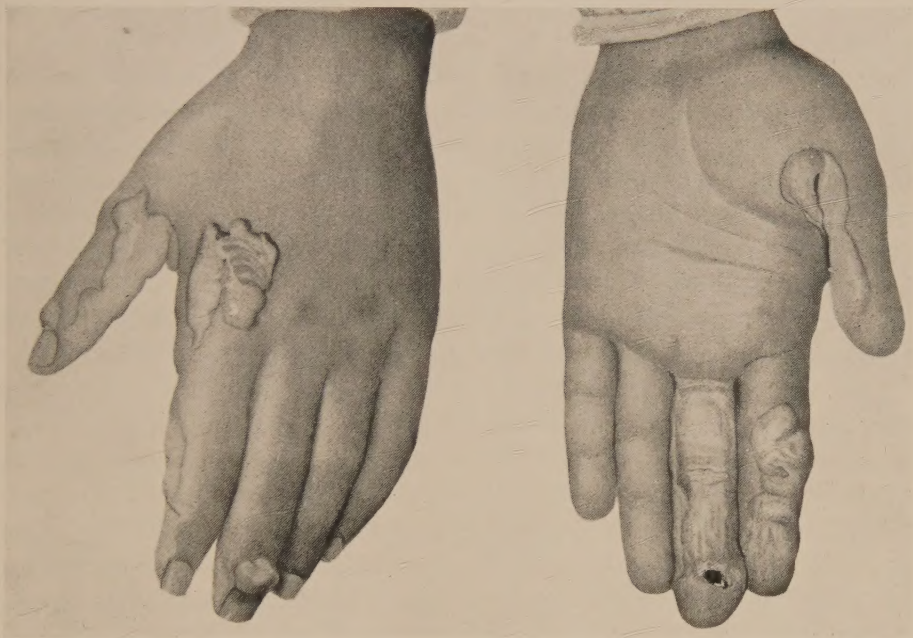

Fig. 3.

character. The histology performed in Radcliffe-Crocker's case was neither diagnostic nor helpful, showing only fibrosis of the corium. Thus a clinical term for a dermatosis showing a persistent erythema was coined without elucidation of the real nature of the condition. It may be noted that it was actually Hutchinson himself who identified Bury's and Radcliffe-Crocker's cases with one of his own and prompted Radcliffe-Crocker and Williams to write their paper.

In the same year Smith (1894) described " a case of erythema elevatum diutinum " in a girl aged 18, who for five years had, on the arms, raised circular or oval lumps, firm to touch, of blue colour and congested in colour and appearance, apparently situated in or just below the epidermis and movable over the

subjacent tendons or fasciae. The epidermis was unbroken and the lesions never ulcerated. The change began with aching pains, then white spots appeared which gradually thickened and became enlarged. There was no history of trauma in any of the lumps. The histology showed nothing except densely matted fibrous tissue, with no cells or nuclei.

In 1895 Hutchinson reported yet another case of a 25-year-old man with a family history of gout who presented an eruption of whitish tubercles, papules and nodules of " fibroid structure " arranged in groups in " psoriatic positions " and in addition on the ears and fingers. The nodules were ill defined, but others coalesced to form distinct rings. (This case could have been granuloma annulare.)

The confusion started when, in the same year, Colcott Fox (1895) showed a case of " ringed eruption on the fingers " in a girl of 11 with a history of aching in the shoulders on walking. On the flexor aspect of the left ring finger and on the right little finger there was a ringed eruption characterized by a smooth, rounded, projecting border, white in colour, doughy in consistency, quite an eighth of an inch wide, and about one sixteenth of an inch in height. The enclosed area was normal, or perhaps a little reddened, and slightly tender on pressure. Colcott Fox was at a loss regarding the diagnosis. No biopsy was performed and he regarded the case as " an indolent form of inflammation, associated with rheumatism and allied to the eruption described by Radcliffe-Crocker as erythema elevatum diutinum."

In that year Dubreuilh (1895) described a case of " chronic circinate eruption of the hand ", and referred to Colcott Fox's case. Clinically the lesions consisted of firm pale elevations on the radial border of the two index fingers and on the ulnar border of the left thumb. For the first time a clear histological description of granuloma annulare was given ; a central focus of necrosis of the collagen surrounded by histiocytes was described.

Galloway (1899) described what appears to-day to be a classical case of granuloma annulare under the name of lichen annularis. The histology showed central necrosis surrounded by an inflammatory reaction. Galloway was not sure how to classify the condition, although he recognised the clinical and histological similarity to Dubreuilh's case. He thought that the cases described by Hutchinson, Bury and Radcliffe-Crocker were due to gout and rheumatism, producing lesions marked by congestion and oedema with less regular distribution than other cases in which the influence of gout or rheumatism is more remote, and suggested that " other causes, the exact nature of which are not understood, are capable of producing a group of eruptions very similar to those associated with gout or rheumatism, but less erythematous and more regular in their distribution ". It is clear from his resumé (1902) that he did not recognize a difference between these conditions.

Radcliffe-Crocker (1902) published a paper on 6 cases of granuloma annulare,

giving this well-defined entity a name. He stated : " Nodules or papules of slow development which tend to form circles by aggregation or partial coalescence, leaving the components still visible ". The nodules are firm, of violaceus red or pale colour with a tendency to involution. The nodules may show a warty character or may be flat or rather suggestive of lichen planus. The distribution is chiefly on the wrists and dorsa of the hands and fingers, but also on the neck and, in four of his cases, on the nape near the hairline. The histology of one case, however, did not show the histology as we know it to-day but a simple " granuloma ". As Radcliffe-Crocker refers to the warty appearance of some of his cases and as the case biopsied had warty lesions, it may be doubted whether some of these were actually granuloma annulare, particularly since he stated that " in two cases there were common warts both as antecedents and concomitants " and one " went on to a condition like lupus verrucosus ; but the histology lends no support to their being of a warty character, the epidermic changes being trifling compared to the copious cell-infiltration of the corium ". As a further complication Radcliffe-Crocker did not regard Dubreuilh's case as being granuloma annulare. He did, however, describe granuloma annulare as a clinical entity, and did not regard it as identical with his erythema elevatum diutinum.

Audry (1904) described the case of a boy aged 9 years who developed on different parts of the body erythematous lesions which became fixed, and changed on the elbows and backs of the hands into hard plaques and nodules. At the same time bullae appeared which developed on previously unaffected skin. The histology showed acanthosis of the epidermis, increase of blood vessels with swelling of their endothelial linings, and a perivascular infiltration consisting of round cells, plasma cells, mast cells and polymorphs. Within the cutis there was sclerosis in some places. Audry gave the case the purely descriptive name of *erythematosclerose* to imply that the condition is an erythema tending to undergo fibrosis. Because his case also showed blisters he added the word *pemphigoides*.

It is interesting to note what Graham Little said about erythema elevatum diutinum in his article on granuloma annulare (1908) : " It will be noted that I have excluded from my list a series of cases recorded by Jonathan Hutchinson ... No histological investigation of these cases was made ; the notes are scanty ; and the clinical facts observed do not, to my mind, justify their inclusion in the same category as the cases I am about to describe, while the absence of histological detail leaves their nature quite problematic ". In another place he says : " the exact relation of ' granuloma annulare ', or of the group of cases named by Crocker, ' Erythema elevatum diutinum ' is very difficult to determine, especially as no accepted case of the latter has appeared at any of the Dermatological Societies for many years ". He said that " the description of the case which formed the basis of Crocker's paper

reads much like the condition seen in granuloma annulare on the *histological features** of a deep seated inflammation of the corium, with fibrous changes resembling keloid ".

It is seen, therefore, that although Graham Little discarded Hutchinson's cases as not belonging to granuloma annulare at all, he is prepared to accept Radcliffe-Crocker's case on histological evidence as a case of granuloma annulare, pointing out at the same time Radcliffe-Crocker's doubt as to the identity of erythema elevatum diutinum with the latter condtion.

In 1910 Dalla Favera set up for the first time a clear dividing line between erythema elevatum diutinum and granuloma annulare. He described three cases.

His first case was that of a farmer aged 23 who developed a rash on the limbs with general malaise and pains in the joints. The rash, which lasted 5 months, consisted of pea- to bean-sized grouped, elevated pale nodules, some covered by a haemorrhagic crust and some eroded, discharging a scanty fluid. The nodules were hard, some warty and containing a haemorrhagic point ; they were localized on the elbows, backs of hands, knees, ankles and feet. The nodules hurt and irritated and, in addition, there was purpura of the legs. The histology revealed acanthosis of the epidermis with vesicles containing red blood cells and polymorphs. Within the cutis there was a marked infiltration consisting of polymorphs, eosinophils and macrophages containing debris. Many polymorphs had undergone necrosis, but actual abscesses were not found.

The second case was of a man aged 38 years " exposed to rheumatic influences " who developed pains in the joints accompanied by an eruption of large nodules localized about bony prominences on the hands. Again, there was purpura of the legs. The histology was the same as in the first case.

His third case was typical granuloma annulare, both clinically and histologically. The illustration accompanying his paper illustrates quite well the clinical and histological features of both conditions.

Zweig (1911) described a man aged 46 who developed ten to fifteen nodules on the forearms and extensor and flexor aspects of the wrists, about $1\frac{1}{2}$ cm. across and arranged in rings. The patient attributed the dermatosis to work in cold surroundings. The histology was not enlightening and the case must be regarded as dubious.

Piccardi's case (1912), however, showed quite characteristic features: A man aged 20 exposed himself to cold water while working at the bottom of a well for several hours. He developed swelling of both knees, legs and feet, with severe pain during the day which disappeared at night in bed. An eruption appeared, involving the scrotum, glans penis, backs of hands, elbows, knees, feet, cheeks and ears, which consisted of white, hard, flattened nodules which showed a tendency to disappear at night and reappear during the day.

* The italics are mine.

There was pain and burning which increased towards the evening. The lesions were of cartilage-like consistency and keloidal appearance. On the cheeks and ears the papules were urticarial, and the glans penis showed a round lesion, centrally umbilicated, with the edge composed of little blisters containing serum. The eruption showed different stages, some lesions being flat with a smooth surface, some desquamating, and some verrucous with punctate bleeding. In many places the eruption was situated over bony prominences and in the vicinity of tendons. A striking clinical feature was the fact that, although the lesions had a keloidal appearance, they flattened in the warmth, only to recur in the same places after exposure to cold.

Frühwald (1916) described a case of a man 60 years old, with an eruption on the forearms, backs of hands, lower legs and feet consisting of lentil-sized, bright red, indurated nodules, which did not disappear on diascopic pressure. The red-brown nodules were either solitary or in groups and rings, with superficial scaling. They became brown as they resolved, the pigmentation slowly disappearing centrally and leaving a coloured ring. The patient also showed large half-lemon sized bluish red to brown tumours with a verrucous or scaly surface. There was a burning sensation in the mouth, with a little ulcer of the uvula. The histology revealed the chief changes to be confined to the cutis and to consist of a diffuse and perivascular infiltration of round cells and polymorphs. In the centre there was an increase of fibroblasts leading to fibrosis. The elastica was missing in the infiltrated areas. Frühwald pointed out that the condition was inflammatory with a tendency to fibrosis. There was no necrosis to be found and that clearly differentiated the case from granuloma annulare.

The history of this entity therefore started with Hutchinson, Bury and Radcliffe-Crocker who described a group of dermatoses which were characterized by their erythematous nature and by a tendency of some of the lesions to undergo fibrosis. Hutchinson was responsible for identifying Bury's and Radcliffe-Crocker's case with one of his own, but his evidence was based on a drawing of Bury's case. Gout and rheumatism were held responsible for the condition. No histological examination was carried out either in Hutchinson's or in Bury's case and Radcliffe-Crocker's histological report of his own case is very poor and not diagnostic. The authors gave the condition non-commital and purely descriptive names: Symmetrical purple congestion of the skin (Hutchinson); erythema with remarkable thickening and induration of the skin (Bury); erythema elevatum diutinum (Radcliffe-Crocker).

When at the same time the first reports appeared on the condition known to-day as granuloma annulare, considerable interest arose as to the identity and relationship of it to Radcliffe-Crocker's disease.

Colcott Fox regarded it as "allied" to erythema elevatum diutinum; Galloway was uncertain; and Radcliffe-Crocker, by creating a new entity,

separated the two conditions. Graham Little, discarding Hutchinson's cases, regarded Radcliffe-Crocker's case as probably identical with granuloma annulare on histological grounds. In France, Audry summed up the situation by calling both conditions *erythematosclerose*—again a non-commital, purely descriptive term. Brocq simply classed the condition under erythemas (1907).

Dalla Favera was the first author to set out the fundamental differences between the two conditions. Erythema elevatum diutinum shows an acute inflammation of the cutis consisting of polymorphonuclear infiltration and no changes in the collagen ; granuloma annulare shows essentially a necrobiotic process of the collagen surrounded by a foreign-body reaction with a peculiar palisade arrangement. His paper was followed by two others (Piccardi, Frühwald) which fully confirmed these findings.

Curiously enough, this lead was not followed up ; later cases and reports appeared which were not accurately diagnosed. Apparently Favera's paper was completely ignored and erythema elevatum diutinum was regarded as an obscure condition at least allied to granuloma annulare. (Bunch, 1918 ; Goldsmith, 1927, 1928 ; Gray, 1931 ; Trimble, 1926 ; Carleton, 1931 ; Lipman Cohen, 1948.)

Weidman and Besancon (1929) published a paper on erythema elevatum diutinum, in which they write : " From the original description of the condition by Crocker and Williams in 1894, it appears that the English are best acquainted with the disease and that, except for Trimble's formal report, none has been made elsewhere either in American or Continental literature ". This at least shows that they wrote their paper quite independently of those written by Dalla Favera, Piccardi and Frühwald—a fact which enhances the value of the article, since it confirms the findings of the previous three authors.

Their first case concerned a man of 35 with an eruption of nodules and plaques of a faint orange hue, distributed over the knees, malleoli, tendo Achillis, elbows, ulnar protuberance and knuckles which had been present for nearly three years. The infiltration waxed and waned and at times some lesions completely disappeared leaving hyperpigmentation of the skin, only to reappear later. Because of the colour and distribution of the lesions they were regarded at first as xanthoma tuberosum. The second case was of a woman aged 34 with brownish-red, infiltrated plaques over the legs, knuckles and elbows. In addition there were numerous areas of pigmentation on both legs below the knees which were regarded as having been the sites of previous lesions. As in the first case, the plaques waxed and waned, and on occasion, were painful. The histology in these two cases was similar and, in the authors' opinion, pathognomonic and hitherto undescribed.

In the first case the epidermis showed a thick stratum corneum, granulosis

and slightly swollen prickle cells with distinct prickles and widening of the intercellular spaces. The important change was in the corium, which exhibited a marked perivascular infiltration consisting predominantly of polymorphonuclears, with few eosinophils and round cells. The cells were present in goodly or large numbers within the walls of vessels, but it was around them that the greatest numbers occurred. Pus formation could not be found, although disintegration of leucocytes was seen in some places. The perivascular infiltration was so extensive that individual foci fused to cover large areas of the cutis. The changes were seen in greatest intensity in the subpapillary region, but reached the level of the sweat glands. A further characteristic feature was the thickening of the perivascular reticulum by hyaline degeneration. The authors called the change " toxic-hyaline " and remarked that the degree of this change will fluctuate according to the stage of the lesion. The second case showed a similar histology, but the changes in the vessels were not so obvious as in the first case.

Bloom (1938) showed a case of erythema elevatum diutinum which was histologically accepted by Weidmann and published two years later by Coombes and Bluefarb (1940).

Engmann, Pfaff and Cooper (1942) reported a case which histologically and clinically conformed with those published by Weidmann and Besancon. Two biopsies taken at six-monthly intervals emphasized the importance of repeating investigations which may at first be of no assistance. The first showed a marked hyperkeratosis of the epidermis with thickening of the granular layer and a moderate degree of acanthosis ; the corium showed a dense infiltrate, especially in the upper portions, which consisted largely of lymphocytes and epithelioid cells. Only an occasional polymorphonuclear leucocyte was found. There were also small deposits of basophilic granular material in the upper cutis, some of which had been engulfed by the phagocytic cells of the infiltrate. This material gave a positive reaction for iron, and could have been the remains of red blood cells which had undergone degeneration. The superficial blood vessels of the cutis were dilated and their endothelial linings hyperplastic. The second biopsy showed little change in the epidermis, but in the cutis there was oedema of the collagen and dilatation of the lymph spaces ; throughout the corium, especially around blood vessels, sweat glands and ducts, there was a conspicuous infiltrate consisting of large numbers of polymorphonuclear leucocytes and epithelioid cells, some fibroblasts and a few lymphocytes. This infiltrate was scattered between the collagen bundles throughout the entire thickness of the corium and into the subcutaneous fat, but was more dense in the upper third of the dermis and surrounded the blood vessels in a relatively thick collar. The walls of the blood vessels showed oedema with some hyalinization and the lining endothelial cells were hyperplastic and their nuclei swollen. The lumina of some of the vessels were obliterated.

It is evident that the disease cannot be definitely excluded by a single biopsy, even of a typical clinical lesion, since the histological appearances vary according to the age of the lesion and may not be diagnostic.

In 1944 Ketron described a case of erythema elevatum diutinum which he was able to follow clinically and histologically for nine years. The patient had mild arthritis of the spine, fingers and one knee. She had marked pyorrhoea involving three teeth, and chronic tonsillitis. His illustrations perfectly demonstrate the course of the disease. The lesions would come and go in the same area and they were worse in the afternoon than in the morning, being more elevated, more highly coloured and associated with pain similar to that which one experiences from being pinched. He performed five biopsies which showed different stages of the pathological process. Three were taken in 1936, one 1938 and one 1943. The first biopsy showed a few vessels partly or completely surrounded by a dense mantle of polymorphonuclear neutrophils with an occasional lymphocyte. In some cases the walls were oedematous and disrupted by invading leucocytes which, with swollen and proliferating endothelial cells, almost obstructed the lumen, but thrombi could not be identified. A few polymorphonuclear cells could be found also in the tissue spaces. Other vessels showed dilatation and perivascular round-cell infiltration. The second biopsy showed ten or twelve blood vessels with very marked perivascular infiltration of polymorphonuclears and severe " toxic-hyaline " changes like those described by Weidmann and Besancon. The walls and a wide margin of surrounding connective tissue had been replaced by an irregular network of coarse eosinophilic fibres. At the periphery of the lesion the vessels showed a perivascular infiltrate consisting of round cells, neutrophils and a few eosinophils. The lower parts of the cutis were normal.

The third biopsy showed changes affecting the entire vascular network, with endothelial proliferation leading to occlusion of vessels. Perivascular infiltration with neutrophils was intense, reaching right down to the fat tissue, and " toxic-hyaline " changes in the perivascular tissues were conspicuous. There were also changes in a few sweat glands. The elastica was destroyed at the places of infiltration around blood vessels. The fourth biopsy, taken two years later, still showed perivascular infiltration with neutrophils, nuclear fragments and macrophages containing red cells and mild " toxic-hyaline ". The striking feature, however, was the advanced fibrosis of the corium, which was complete in the fifth biopsy five years afterwards. Here the lesion consisted of a richly cellular fibrous nodule containing mostly connective tissue cells and lymphocytes with a few polymorphonuclear leucocytes scattered here and there. The small vessels were thickened ; a few were patent, but the majority appeared as solid cords of connective tissue. There was no evidence of toxic-hyaline and the elastica had disappeared entirely.

A case shown by Schweig (1944) was diagnosed histologically by Klemperer

Fig. 4.

Fig. 5.

as erythema elevatum diutinum. There were bullae as well as nodules, strongly reminiscent of Audry's and Piccardi's cases.

Combes, Behrman and Saperstein (1948) described two cases of erythema elevatum diutinum ; although they were still hazy about the clinical concept, they set out a clear histological delineation between the two conditions :—

Erythema elevatum diutinum = an acute tissue process.
Granuloma annulare = an extensive necrotic process with subacute to chronic reactive inflammation.

Weiss, Cooper and Gottschalk (1948) reported three clinically and histologically typical cases.

In 1950 Haber and Russell presented a case to The Royal Society of Medicine. The lesions were paler and in most places were skin-coloured or pink instead of the brownish-red colour which seems to have predominated in most other cases. Furthermore the eruption was much more profuse, consisting of a very large number of small lesions, and itching was a prominent feature.

Case Report.

A woman aged 53 was first seen at hospital on 7.x.1952 (MacKenna *et al.*, 1953).

Past History.—She states that she had chorea at the age of four years, but in view of the rarity of the disease at this age this must remain doubtful in the absence of confirmation. She has been nervous and run down for some time and has nervous tics. The family history is irrelevant. The eruption started about 9 months ago on both knees with a bruise-like discoloration, which spread to both legs and to the points of the elbows.

On Examination.—When first seen she had an eruption on the points of the elbows, hands and fingers, knees, the whole of both legs from the knees downwards, the ankles and the dorsa of the feet and toes (Figs. 4 and 5). The eruption was composed of nodules, aggregations of nodules, many of which were arranged in lines looking vaguely like indurated lymphatics or veins, and plaques, which were raised about $\frac{1}{10}$ inch from the surrounding skin (cf. Hutchinson's case). The nodules varied in size from about $\frac{1}{8}$ to $\frac{1}{3}$ inch in diameter, the majority being smaller and somewhat flattened ; the larger ones were more spherical and were found particularly on the knees, elbows, heels and dorsa of the toes. Many of these larger nodules were covered with scabs and often haemorrhagic. The colour of the lesions varied considerably, and while most of them were of a reddish-brown colour, a few were more purplish, and many of them had a distinct pale yellow colour. This yellow colour was particularly well marked over the knees and shins when the patient was first seen (as in Bury's case). If the reddish colour was expelled from the lesions this same pale yellow colour was seen underlying it. The surface of most lesions was smooth and without scaling. All the lesions felt hard and could be lifted up from the tissues beneath. A tentative diagnosis of xanthoma tuberosum was made and a biopsy performed.

Within a few weeks of first being seen many of the lesions, particularly those on the legs below the knees, had flattened and disappeared, leaving only a residual brownish pigmentation. Three weeks later, however, many of these same lesions had once again become raised and yellow, and she began to complain of pain in the legs, knees and hands at the site of the nodules and plaques. In the legs and

hands it was of an aching nature, but in the elbows shooting pains also occurred. Some weeks later a further change was seen, the nodules on the left knee having fused into brownish-purple plaques with a firm, raised, bright yellow edge. As this raised edge advanced the plaque behind it flattened out. It was noted by now that the yellow infiltrations were more variable and the purple ones were more stable, but one could never be quite sure whether the yellow colour merely represented a certain active phase, or whether some lesions were yellow all the time and others never. (Ketron (1934) had the impression that in his patient the yellow colour was related to the degree of infiltration.)

By 12.xii.52 the pain was causing considerable distress and she was given a mild analgesic without, however, much effect. A course of aureomycin was then administered (250 mg. 6-hourly for 2 weeks), but severe diarrhoea necessitated its

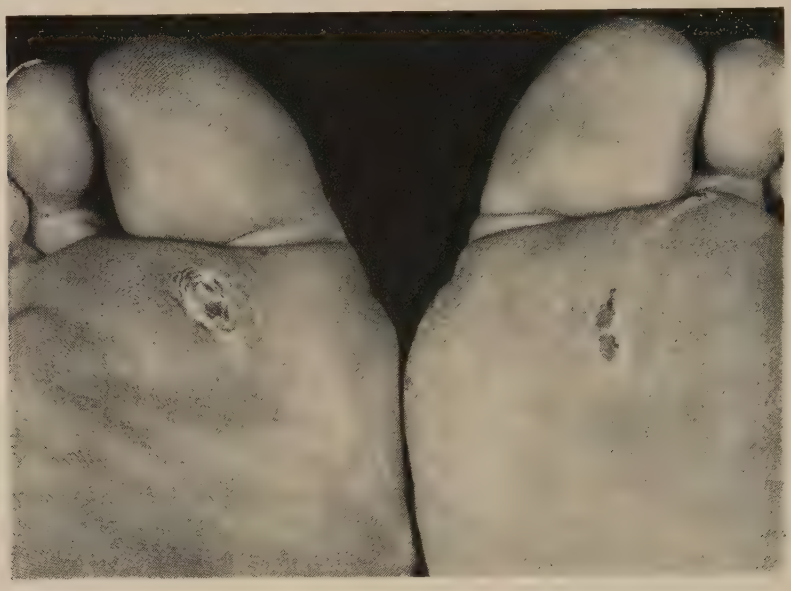

Fig. 6.

withdrawal. Two weeks after this there was a further change in the clinical picture, though whether this was due to the aureomycin one cannot say. Almost all the yellowish infiltration had disappeared and on the legs many of the plaques and nodules had flattened, leaving a reticular pattern similar to that of livedo racemosa, brownish-red and still slightly raised in some parts, but in others nothing but a brown pigmentation. There were still a few small yellow nodules on the elbows, some of which looked extraordinarily like the so-called pustular eruptive xanthomata. A very large number of nodules, especially on the feet, hands, knees and elbows were now covered with crusts, many of which were haemorrhagic. It had been thought at first that the few crusted lesions originally present were the result of trauma, but it was now obvious that this was not so. (A similar spontaneous crusting was reported by Engman, Pfaff and Cooper in their case.) When the patient was last seen in March 1953 there had been little further change in the condition, despite superficial radiotherapy. Fresh lesions had appeared on both buttocks and on the soles, where they closely resembled plantar warts (Fig. 6).

Histology.—In the first biopsy the epidermis shows a slightly thickened stratum

corneum both of the loose and of the compact type overlying a single layer of granular cells and an acanthosis with intra- and intercellular oedema. In one place this has led to the formation of large vesicles immediately above the basal cell layer which is intact and is sharply demarcated from the underlying corium. Separated from the epidermis by a thin band of oedematous and almost acellular collagen, there is a very dense infiltration, which extends right down to the upper parts of the subcutaneous tissue (Fig. 7). The infiltrate has invaded the collagen between the

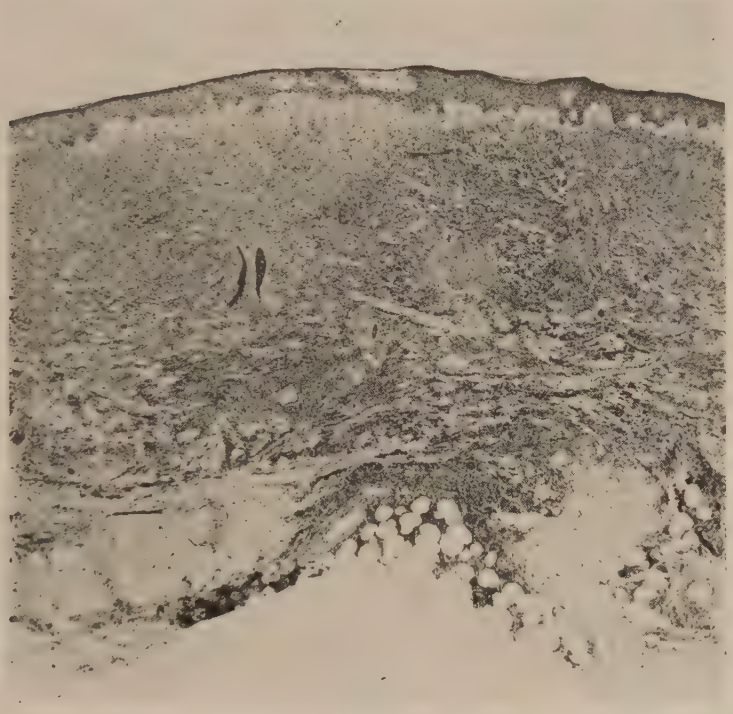

Fig. 7.

tissue spaces, breaking it up into isolated bundles (Fig. 8). It consists chiefly of polymorphs, although there are also lymphocytes and a conspicuous number of eosinophils. In the upper part of the inflammatory area there is some disintegration of polymorphs, but actual pus formation does not take place. In the upper parts of the corium are small vessels with apparently thick walls, an appearance which on close inspection is seen to be brought about by a coarse perivascular reticulum (Fig. 9). The walls are penetrated by the infiltrate and have a hazy outline. Further from the infiltrate the corium is scantily infiltrated with lymphocytes, many polymorphs and a few eosinophils. Several small blood vessels show a peculiar segmental infiltration of their walls. In the deeper parts of the corium other vessels show different degrees of proliferation and obliteration.

A second biopsy performed on a fibrotic lesion is shown in Fig. 10. On the left side one can see the characteristic acute infiltration as in the first section. On the right side there is considerable fibrosis with a few scattered polymorphs, the rest of the cells being round cells and fibroblasts. The section, therefore, shows the classical picture of acute inflammation and fibrosis side by side, and it also explains

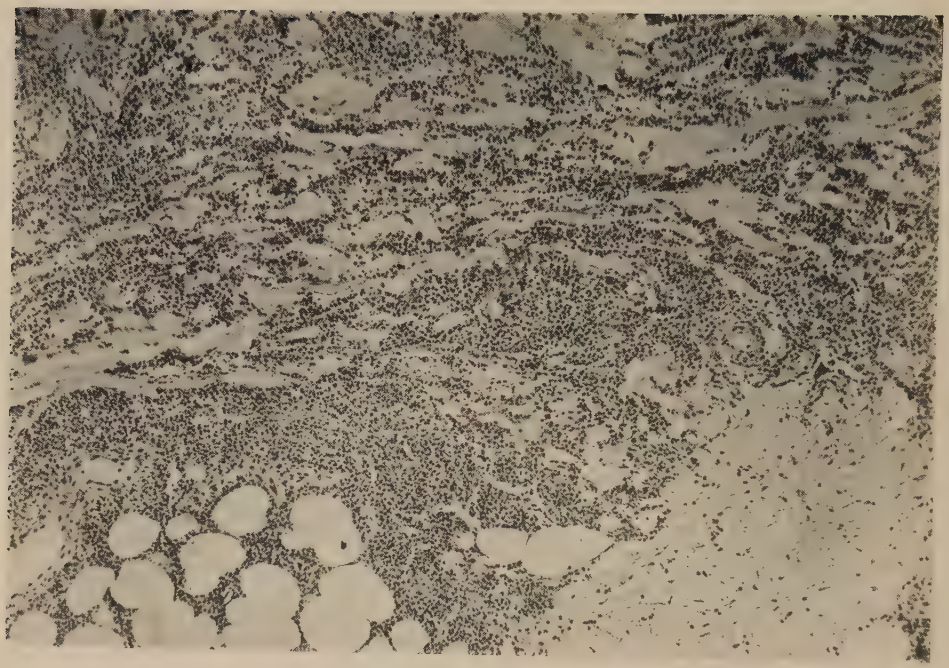

FIG. 8.

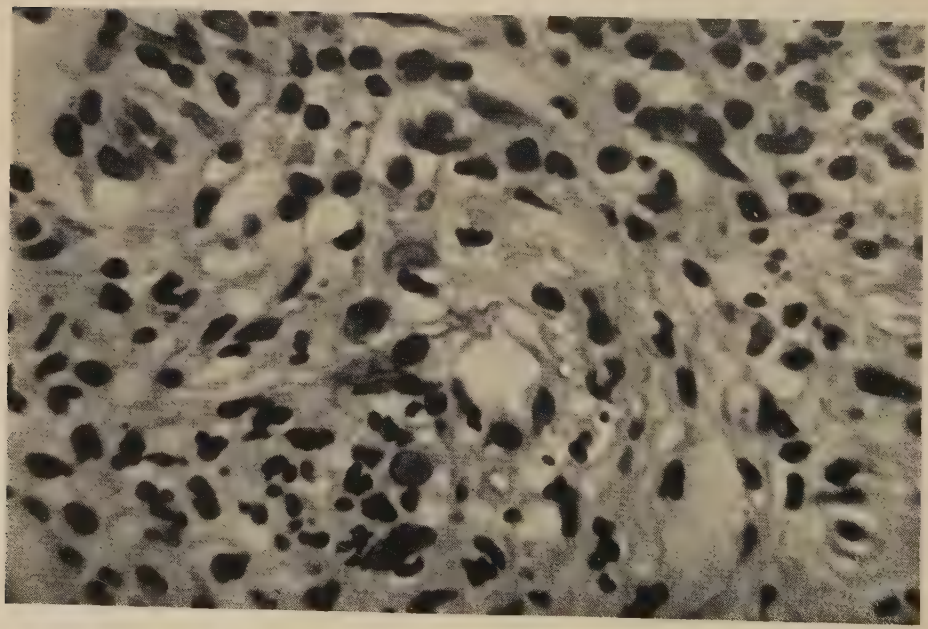

FIG. 9.

how apparently fixed fibrotic nodules may show an evanescent character. It is due, apparently, to the fact that the inflammatory infiltrate which blows up the fibrotic nodules may temporarily subside and lead to a considerable flattening of the lesion, which again enlarges when relapse of the inflammation recurs.

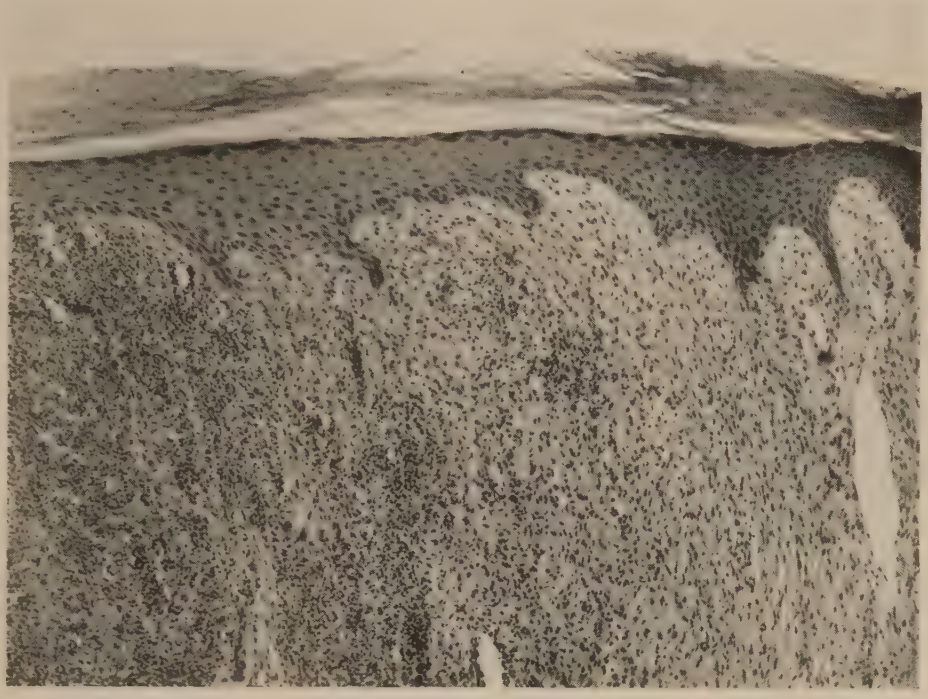

Fig. 10.

Other investigations—

Blood Cholesterol, 280 mg./100 ml.
Blood Sugar, 85 mg./100 ml.
W.R. and Kahn, negative.
Urine, normal.
Blood Count: R.B.C. 4,610,000: Hb 96%: W.B.C. 6500: polys. 62%, eos. 2%, lymphos. 34%, monos. 2%.
Skiagrams of the humerus, femurs, tibiae and fibulae, pelvis, ribs and skull revealed no abnormality.

Clinical Summary.

It would be pertinent, before discussing erythema elevatum diutinum, to consider briefly the clinical and histopathological features of granuloma annulare.

That condition is more common in children and young adults, but may occur at any age. The eruption consists of skin-coloured papules which enlarge and, by spreading and central delling, produce characteristic rings. At other

times the rings are made by a group of papules. The lesions are to be found on the backs of the fingers and hands, toes and feet, extensor surfaces of the elbows and knees, and sometimes on the thighs, buttocks, breasts or face. They may also lie deeper within the corium and then the morphological appearance is not so characteristic. Indeed, the morphology may vary considerably and a generalized form is recognized also. Civatte (1952) recently described an ulcerative form. Fig. 11 shows a typical lesion. There is a central area

Fig. 11.

of degeneration of collagen surrounded by a histiocytic reaction, the histiocytes being arranged in a pallisade manner pointing towards the degenerated area. Round cells add to the infiltrate and many histiocytes may fuse to produce small giant cells. Blood-vessel changes as a rule cannot be found, but both mucin and fat are sometimes observed. Depth, extension and severity of necrosis vary considerably in individual lesions giving slightly different pictures, but the fundamental changes remain the same: necrobiosis or necrosis of collagen with a characteristic cellular reaction. The lesions may clear up histologically and leave no trace, or, when the necrosis is extensive and severe, repair will take place by fibrosis giving a histological picture which is not at all characteristic. In this way the histology of granuloma annulare may vary considerably.

It is quite clear that the cases described as erythema elevatum diutinum are something quite different, both clinically and histologically. The condition occurs usually between the ages of 30 and 60 and affects either sex in equal proportions. The oldest and youngest cases reported are 64 years and 5 years respectively.

The lesions themselves may be either papules or nodules, varying in size from 3 mm. to a centimetre or more in diameter, or round or oval infiltrated plaques up to 5 or 6 cm. across. The thickness of the plaques varies ; in some cases they are raised almost $\frac{1}{4}$ inch and in others so slightly that the lesions resemble erythema multiforme except for the colour. These plaques may arise *de novo* or may consist of aggregations of papules or nodules, in which case annular, circinate, or even bizarre streaks are sometimes formed. The smaller lesions, while still remaining more or less discrete, may also be arranged in lines. In most cases both nodules and plaques are seen, but occasionally either type of lesion may occur alone.

The colour varies considerably even in the same patient, and although the majority of the lesions are reddish or purplish with a distinct dusky brown undertone, a yellow, yellowish-brown, or even distinct orange colour is seen frequently enough to form one of the characteristic features of the disease and to have led in more than one instance—as in the case reported here—to a provisional diagnosis of xanthoma tuberosum.

The surface of the lesions, which in most cases is quite smooth or with only minimal scaling, may become verrucose and covered with crusts, many of which are haemorrhagic and arise quite independently of trauma. The haemorrhagic nature of these crusts, when present, is highly characteristic of the condition. Some cases may also exhibit purpura.

Itching has been described, but it is not a characteristic feature of the condition, although complaints of pain in the nodules or plaques are not unusual. It has been variously described as an aching, burning, tickling, throbbing or bursting feeling, or a sensation similar to that experienced from being pinched. It is, as a rule, inconstant and tends to be more severe towards the end of the day ; it may be sufficiently severe to be a source of considerable suffering.

The distribution of the lesions is a characteristic feature. They usually tend to be grouped in the neighbourhood of the joints, both large and small, and affect therefore mainly the backs of the hands and fingers, wrists, elbows, knees, ankles, toes and over the tendo Achillis. Other sites not infrequently affected are the legs below the knees, the buttocks and, less often still, the forearms, nose and ears, and penis. The trunk is almost invariably spared.

The condition is essentially chronic and progresses, in most cases over a period of 5–10 years, to eventual resolution, although involution within a shorter period may also occur. During this time the clinical picture usually

undergoes certain variations. Thus, while some lesions disappear completely fresh ones may appear, and existing ones not infrequently extend in one place and regress in another. One of the most characteristic features of this variable picture, however, is the tendency for certain lesions apparently to resolve completely over the course of many weeks only to reappear at a later date in exactly the same places. Change of temperature, and especially cold, seems to aggravate the lesions considerably. Residual pigmentation is common, although by no means invariable, and seems to be most marked on the lower legs. Apart from this pigmentation, however, the skin is left quite normal, although slight atrophy has been described.

Histopathology.

The first author to report on the histology of the condition was Radcliffe-Crocker. Unfortunately his findings were very scanty as the biopsy revealed only a fibrotic process. Smith found absolutely nothing, and at first one might assume that the cases reported were probably not true examples of erythema elevatum ; but as will be shown later, they can nevertheless be accepted. Audry was the first to report subacute inflammatory infiltration of the cutis with a tendency to fibrosis. Favera clearly saw the acute inflammatory condition of the cutis in two cases. The infiltrate consisted of polymorphs, eosinophils and macrophages. The interesting feature was the absence of abscess formation, although a few leukocytes showed fragmentation of their nuclei. Dalla Favera pointed out that it was surprising to find an acute inflammatory reaction of the cutis in an apparently chronic condition. He submitted that the process in the cutis was the result of a chain of consecutive episodes of acute inflammatory reactions, a pathology quite distinct from granuloma annulare. His findings were confirmed by Piccardi and by Frühwald. But Piccardi, although pointing out the different histological pictures, concluded that the aetiology in both conditions might be the same. There followed a period of confusion which was resolved by Weidmann and Besancon, who, without knowledge of previous papers, clearly defined the clinical and pathological condition of erythema elevatum diutinum. The fundamental pathology of the condition is an acute periarteriolitis and peritelangitis in the corium.

The infiltrate will consist, according to the age of the lesion, chiefly of neutrophils, eosinophils, round cells, plasma cells and macrophages containing nuclear debris and sometimes iron. The infiltrate is chiefly perivascular, but it can also be seen to spread between the tissue spaces, where the cells are arranged in long rows. A further feature is the change in the blood vessels which may vary considerably according to the age of the lesion. There may be only swelling of the endothelial lining, the lumina may be narrowed or even

occluded, but thrombosis does not take place. The perivascular reticulum of small vessels may undergo considerable hypertrophy and change of staining properties, the fibres attaining a brilliant eosinophilic colour. This change was called by Weidmann "toxic-hyaline". It occurs only in advanced lesions and was not present in our case. Ketron has clearly shown how, after a long period, the collagen undergoes complete fibrosis to produce clinically the characteristic nodules. This feature has been observed in the majority of cases. In our case the nodule showed on the one side an acute inflammation and on the other fibrosis with many neutrophils, thus showing how waves of polymorphs can produce a flare-up in a clinically solid nodule. The epidermis shows changes which are secondary to the changes in the corium ; there may be acanthosis only or, according to the activity of the inflammation, oedema and vesiculation, with vesicles containing serum and blood which lead clinically to verrucose haemorrhagic nodules. The whole process is in accordance with Favera's concept, consisting of a series of acute inflammatory episodes in the cutis leading to blood-vessel changes, secondary changes in the epidermis, and ultimately, on healing, to complete fibrosis and the formation of hard nodules. This being the case, one can do away with the concept of a Bury type and Hutchinson type of the disease and regard the condition as one dynamic, continually relapsing process, terminating with fibrosis.

Looking back to the first reports by Radcliffe-Crocker and Smith, it may be thought that the fibrosis found in both cases represents the terminal stage of the condition. Since severe granuloma annulare may also terminate with fibrosis, the confusion of the two conditions can be understood.

Discussion.

Having now established a clinico-pathological entity, there remain four questions to be answered.

(i) Are these cases identical with Radcliffe-Crocker's original case ?

(ii) Is the pathology unique and pathognomonic ?

(iii) What is its nosological position ?

(iv) What is its relationship to rheumatism ?

(i) Ketron stated that owing to the brevity of the histological study by Radcliffe-Crocker a certain identification is impossible. He suggested, therefore a fresh start with the description of Weidmann and Besancon as a nucleus, and proposed to borrow the name erythema elevatum diutinum temporarily.

On reading Bury's brilliant account of the clinical features of his case, one cannot help feeling that this was the first description of erythema elevatum diutinum. There is no need to stretch one's imagination to see that the picture of Ketron's case (Fig. 4 in his paper) hardly deviates from Radcliffe-Crocker's illustration. Hutchinson's fourth case showed " the presence of little cords,

like hardened lymphatics or small veins, running upwards from the diseased parts ", a feature corresponding exactly with our case. The old masters were brilliant clinicians and since it was Hutchinson who identified the first cases as probably identical, *there is reason to assume that the cases under discussion are identical with Radcliffe-Crocker's original concept.*

(ii) The histology shows an acute vasculitis and perivasculitis in the corium, and according to the age of the lesion various changes in the perivascular tissues may occur with an inflammatory infiltrate consisting of polymorphs, eosinophils and lymphocytes. A further feature is the fragmentation of nuclei and phagocytosis. The infiltrate penetrates between the tissue spaces, and as it increases its perivascular distribution may be obscured, leading to a dense acute infiltration of the whole corium and the upper part of the fat. If the lesions persist for a long time fibrosis replaces the infiltrate, leading clinically to the formation of a nodule.

Weidman pointed out that an acute histology in a chronic condition is most surprising, and considered it to be unique in dermal histopathology.

Acute vasculitis is to be found in subacute bacterial endocarditis. Here the histology shows endothelial proliferation in capillaries with narrowing or obliteration of the lumina. Around these capillaries is an infiltrate consisting of polymorphonuclears, lymphocytes and histiocytes. Streptococci have never been found in the lesions (Merklen and Wolf, 1928).

In erythema annulare rheumaticum (Lehndorf and Leiner, 1922) a condition sometimes seen early in cases of rheumatic fever, Carol and Kreeken (1922) found a partly diffuse and partly perivascular infiltrate consisting of neutrophils, eosinophils and lymphocytes. They did not find any organisms in the infiltrate.

In meningococcal septicaemia there is necrosis of the vessel walls, swelling of the endothelial linings, thrombosis, and a marked perivascular polymorphonuclear infiltration ; extravasation of red blood cells may be seen. Meningococci can be demonstrated by Giemsa's stain within endothelial cells, in neutrophils, within the lumina of the vessels in perivascular spaces, and within thrombi (Lever, 1954).

In staphylococcal and streptococcal septicaemia the rashes produced by these organisms produce a severe vasculitis with damage to vessels and marked polymorphonuclear infiltrations, and both staphylococci and streptococci can be demonstrated in sections (Gans, 1921).

In all septicaemic exanthemata the organism responsible can easily be demonstrated. In streptococcal endocarditis and erythema annulare rheumaticum no organisms have been found. This can be explained either by supposing that only a few of them have reached the vessels where they were destroyed on the spot, or that a bacterial toxaemia has produced the acute vasculitis. A third possibility is that the haematogenous dissemination of bacterial protein has sensitized the vessels, resulting in an allergic response.

A classical example of allergic vasculitis is the Arthus phenomenon. This is the consequence of an antigen-antibody reaction in a specific hypersensitivity, and shows the characteristic histological features of severe fibrinoid degeneration of the walls of the vessels, swelling of collagen sometimes causing necrosis, and an acute inflammation with polymorphs which show fragmentation of their nuclei. There is also a considerable extravasation of red blood cells. Storck (1951) considers that the haemorrhage is due partly to vascular damage and partly to an increase in circulating heparin with a diminution of platelets. He also states that purpuric eruptions due to haematogenous bacterial dissemination from septic foci are allergic phenomena. Miescher (1946) is of the same opinion, and points out that fragmentation of polymorph nuclei is indicative of an allergic process as it is to be found in the early stages of an Arthus reaction. It can also be found in abscesses, necrosis and septicaemic conditions. Ruiter's arteriolitis, Gougerot's *maladie trisymptomatique* and purpura rheumatica are probably allergic phenomena of the vessels.

In erythema multiforme "the principal changes in the corium consist of dilatation of blood vessels, extravasation of serum and diapedesis of leucocytes. These may be slight and confined to the papillary layer and subpapillary layers, as in the maculo-papular lesions, or they may be more deeply situated, occupying the whole corium and even extending to the subcutaneous tissue, as in nodular forms. When the corium is deeply involved not only leucocytes but red blood cells may pass out from dilated capillaries and proliferation of fixed cells may be detected in their neighbourhood" (MacLeod, 1933). The same histology has been described by Ormsby and Montgomery (1948) and Lever (1954).

It is, therefore, seen that *the histology of erythema elevatum diutium, although characteristic, is not absolutely diagnostic of the condition.*

(iii) In view of our complete ignorance of the aetiological factors of erythema elevatum perhaps it is futile to speculate on the relationship of this dermatosis to similar conditions on a purely morphological level; *but it seems possible that it may be related to erythema multiforme.*

It differs from the latter only by its chronic tendency to persist and relapse. The apparently chronic character of the condition contrasted with the acute histology can be explained by the conception that it consists of a consecutive chain of inflammatory reactions of the vascular network, probably due to circulating toxins in the blood. Perhaps toxins of bacterial origin may play a part. Weidman and Besancon cultured a low grade streptococcus and were of the opinion that erythema elevatum was due to toxaemia.

One case had marked pyorrhoea and tonsillitis (Ketron, 1944); another case started with an abscessed tooth (Engman, Pfaff, and Cooper, 1942); still another case developed the condition after treatment with penicillin for boils (Haber and Russell, 1950).

In two cases bullae also developed at some stage of the condition (Audry, 1904 ; Piccardi, 1912). This brings erythema elevatum still nearer to erythema multiforme.

(iv) Running through most of the reports of this condition is a persistent implication that " rheumatism " or " rheumatic influence " plays an important part in its aetiology. A multitude of conditions, such as fibrositis, sciatica, muscular rheumatism, neuritis, etc., are included under this heading and little more evidence was put forward by the authors except that the cases were associated with pains in the joints and the muscles. Considering the fact that a number of infective conditions may produce " rheumatic " pains, there is really *little to support the contention that erythema elevatum diutinum is a rheumatic disease.*

Summary.

A case of erythema elevatum diutinum is presented and the relevant literature reviewed.

Erythema elevatum diutinum is a distinct clinico-pathological entity, quite different from granuloma annulare.

The cases so far described are in all probability identical with the dermatoses described by Hutchinson, Bury and Radcliffe-Crocker.

Erythema elevatum diutinum is an erythema which, in clear distinction to other erythemas, shows a tendency to persist and to terminate in fibrosis. The acute histology, contrasting with the chronic clinical nature of the dermatosis, is explained in that the process consists of a series of acute inflammatory episodes probably due to circulating bacterial toxins. This leads to sensitization of the affected blood vessels which respond with an acute inflammation. Some of the lesions heal by fibrosis. Erythema elevatum diutinum is, therefore, a dynamic protracted relapsing dermatosis terminating in fibrosis. With this in mind one can do away with the idea of a Hutchinson and a Bury type of the disease and regard it as a single process which passes through different phases of evolution.

The histology is characteristic but not pathognomonic.

Its relationship to " rheumatism " is dubious.

Its nosologic position is discussed and it is suggested that the disorder may be a variant of erythema multiforme.

Granuloma annulare is a distinct clinico-pathological entity of unknown aetiology. Histologically it consists of a localized necrobiotic process resulting in an inflammatory reaction of a characteristic pattern. If a case diagnosed clinically as erythema elevatum reveals the histological features of granuloma annulare then the case is granuloma annulare and not the Bury type of erythema elevatum diutinum. If this fact is kept in mind confusion should not arise in the future.

I wish to thank Dr. R. M. B. MacKenna for allowing me to publish this case.

Fig. 1 is reproduced from *Illustrations of Clinical Surgery* (Hutchinson, 1878); fig., 2 is reproduced from *Illustrated Medical News* (Bury, 1889): fig. 3 is reproduced from this Journal vol.. **6**, 1; figs. 4–11 were taken by Mr. R. J. Lunnon, A.I.B.P., and I have to thank the Institute of Dermatology, British Post-Graduate Medical Federation, for permission to publish them.

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CHRONIC POLYMORPHIC LIGHT ERUPTIONS TREATED WITH MEPACRINE.

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THE effect of mepacrine on lupus erythematosus may, in Page's (1951) opinion, be due to increased light tolerance. It has therefore been natural to try mepacrine in the treatment of light-provoked skin lesions. Knox *et al.* (1954), Rogers and Finn (1954) and Cahn *et al.* (1954) have seen a favourable response in the majority of the cases treated.

PRESENT INVESTIGATIONS.

In May and June 1954 we treated 11 patients suffering from chronic polymorphic light eruptions (terminology according to Haxthausen, 1919). We chose patients who had been affected for more than 12 months, because in these cases we had a good idea of the spontaneous course of the disorder. No local treatment was given, particularly not with light-protective preparations, and after 48 hours the patients were advised not to avoid exposure to the sun. Four of the patients stayed in hospital, but were allowed to go out in the sun, and the rest were treated as out-patients.

The period of treatment was fairly short, in order, as far as possible, to eliminate spontaneous remissions and to permit observation of relapse. Adult patients were given 200 mg. of mepacrine daily for 10 days followed by 100 mg. for 21 days. One child aged 2 years was treated with 50 mg. of mepacrine daily for 10 days and then 25 mg. for 21 days. This dosage gave yellow discoloration of the skin in seven cases. A single patient complained of headache, but no other side-effects were observed. Blood examinations, including white cell counts, revealed no change or abnormality.

The minimum erythema dose of light (m.e.d.) was measured in the cases of six patients before the commencement of treatment and again immediately before its conclusion. For this purpose we used a mercury arc lamp (Hanau) with three strong spectral lines (2970, 3020 and 3130 Å.) within the most erythemogenic part of the ultraviolet band. No filter was employed, and the lamp was submitted to photometric calibration once a week. The area irradiated was in all cases the middle of the back, this area having not recently been exposed to light. The irradiated fields were 2 by 2 cm. squares,

and the lamp–skin distance 50 cm. The irradiation times ranged from 7 to 180 seconds. The minimum perceptible eythema was read after 24 and 48 hours. As the lowest m.e.d. in all cases was found after 48 hours, only this value has been included.

The individual results have been set out in Table I.

TABLE I.

Sex.	Age.	Duration (years).	Results.	Relapse.	M.E.D. before treatment (secs.).	M.E.D. after treatment (secs.).
F.	17	2	Improved	—	..	..
F.	34	5	„	—	..	..
F.	33	3	„	+	..	..
F.	65	2	„	+	28	56
F.	37	25	„	+	60	60
F.	35	1	„	+	..	..
F.	35	25	„	+	20	60
F.	2	1	„	+	..	..
F.	14	12	„	—	60	60
M.	54	14	Not improved	..	7	7
F.	14	9	„ „	..	120	180

DISCUSSION.

It will be seen in the table that mepacrine had an effect in nine out of the eleven patients treated. The period of treatment was, however, too short, four patients having experienced relapse from 1 to 8 weeks after discontinuation of the treatment. These four were later treated with chloroquine and responded favourably to doses of 250 mg. daily. As criterion of response we required almost complete disappearance of the light eruptions. Just over half of the patients developed a cosmetically embarrassing yellow discoloration of the skin, but no other side-effects were seen. It was because of this discoloration that those patients whose eruptions recurred were afterwards treated with chloroquine.

No relationship was found between the intensity of the yellow discoloration and the clinical response. Such could not indeed be expected, since fluorescent substances generally are stated to increase the susceptibility of the skin to light (Kesten and Slatkin, 1953). The response observed to mepacrine is thus not likely to be determined by the fluorescent effect of the preparation. In three patients the light tolerance (m.e.d.) was found increased 50 to 300%, and two of these had improved clinically.

The above investigations showed no unquestionable relationship between clinical improvement and an increased experimental light tolerance, but the results of treatment are seen to be in accord with those of other workers.

Conclusion.

Treatment of chronic polymorphic light eruptions with mepacrine proved effective in nine out of eleven patients. Prolonged treatment is required, as the effect will last only a few weeks after its conclusion. No side-effects were observed, apart from yellow discoloration of the skin. Treatment with chloroquine seems to give equally good results.

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ROYAL SOCIETY OF MEDICINE

SECTION OF DERMATOLOGY.

President—Dr. Reginald T. Brain.

17 June 1954.

Nodular Vasculitis.—Dr. J. E. M. Wigley and Dr. G. A. Beck.

Mrs. M. B—, aged 57.

History.—In 1950 during total extraction of teeth, she developed " phlebitis " of legs below the knee which persisted for several months and finally cleared up rapidly on resting in hospital. After this she had some swelling of the ankles which subsequently settled. In 1952 less painful but tender nodules started to develop in the lower part of the leg, mainly on the front of the shins. During the last year she has not been very well, with a vague illness consisting of headaches. No details of this are available.

Examination.—Patient was first seen on 30 April 1954, with tender, shiny, indurated areas on the lower leg, tending to coalesce and with several discrete nodules on the back of the calves of more recent origin. The areas were of an off-white colour with a pinkish blue border, and were hard to the touch. Blood pressure at that time was 160/90. Urine N.A.D.

Treatment.—Rest in bed, and Tab. Codein Co. There has been much relief of the tenderness and brilliance of the eruption.

Dr. A. Porter : Could this be merely thrombophlebitis ? I do not know how one can be certain that it is nodular vasculitis unless a biopsy has been done.

Dr. J. E. M. Wigley : When I saw this patient she had a tender shiny thickening of the skin on each shin and some outlying nodules. I have seen a number of old phlebitis cases and it struck me that there was something different about this which closely resembled scleroderma. It seems to fit closely the description generally given of " nodular vasculitis " except that this patient had only a slightly raised blood pressure. We have not had a biopsy done so that the argument will still remain a little uncertain.

Dr. F. Ray Bettley : I suggest that this case is a little unusual in two other respects. Instead of being nodular it is sclerodermatous ; it is rather like a large plaque of induration split into separate parts. The second unusual feature is the seasonal incidence : the patient said she was worse in the winter and better in summer which is unusual in the typical case of nodular vasculitis.

I should also like to mention that in cases of this kind—I accept this as being of the same general type—I have treated some half-dozen people with hydroxyphenylcinchoninic acid over the past two or three years with convincing results.

Dr. D. S. Wilkinson : This is one variety of nodular vasculitis and falls into the same group as Whitfield's erythema induratum in which the lesions are centred around the veins. I think this patient would do well with a firm supporting bandage and it might be worth trying it on one leg at a time.

We can argue too much about terminology. The clinical pattern here is essentially phlebitic, but histologically it would, I think, show very much the same picture as occurs in the other groups of nodular vasculitis.

Small Nodular Disseminated Sarcoid, localized to Light-exposed Areas.—Dr. Theresa Kindler.

Mrs. L. W—, first seen 14 May 1954.

Past history.—She has always been in good health. She has had no major diseases, no persistent cough, eye trouble or swellings of the parotid region. Lately she has been short of breath on exertion. Since girlhood she sunburned intensely on the slightest exposure. Her nose has been thickened and red for some time, but she took no notice, ascribing the change to sunburn.

Nine months ago fairly sudden eruption, first in the V of the neck and on the face, then on the forearms. The patient stated the rash appeared shortly after prolonged

exposure to sun at the seaside. During the winter there seemed to be a slight improvement, but new crops appeared during recent months. There were no general symptoms and no irritation.

Family history.—One son has had extensive psoriasis from childhood. Otherwise nothing of note.

Examination.—The face, V of the neck and dorsal surfaces of the forearms are vividly flushed, suggesting a recent sunburn, and covered with a dense eruption. On the forearms are dark-red, flat, firm papules, in size from a millet-seed to that of a small pea, with a smooth glossy surface. They are partly discrete, partly confluent in lines and garlands, but retaining their individual shape. The upper arms, usually covered by a short sleeve, show no sunburn and are almost free of lesions. In the V of the neck the lesions are harder, closely set and stand out yellowish-brown and shiny against the surrounding red skin. Nearly the whole face and the lower halves of the ears are involved with the striking exception of the areas covered by the hairdressing. The skin is here deep red and dotted with numerous purple nodules and diffuse infiltrated patches. Both diffuse and nodular lesions show on diascopy small dark-yellow foci of infiltrate.

The mucous membranes of the mouth, nose, larynx and pharynx are not affected. The parotid glands, tonsils and superficial lymph glands are not enlarged. Fingers and toes look normal.

Eyes.—No involvement.

General examination.—CNS shows no abnormalities. Liver and spleen not palpable. Abdomen: nothing abnormal. B.P. 170/110.

Skiagram (Dr. Staveley).—Chest is overexpanded. Considerable cardiac dilation, no basal effusion is present. Dense shadows are present at both hila with flocculent extension to the periphery. Conclusion: Appearances are those of sarcoid lung with back pressure in the pulmonary circulation causing dilatation of heart. X-ray of nose, hands, feet: no bony changes seen.

Investigations.—Mantoux reaction was negative 1 100. Wassermann and Kahn reactions were negative. Total serum protein 7·6 gr. per 100 ml. Serum albumen 4·8 g., globulin 2·8 g., A/G ratio 2 : 1·3.

E.S.R. 16 to 23 mm. per hour (Westergren). Blood count: Hb. 13·5 (93%), W.B.C. 7500 per c.c. Polymorphonuclears 71%, lymphocytes 17%, eosinophils 4% monocytes 8%.

Serum cholestorol 196 mg. per 100 ml. Serum calcium 9·8 mg. per 100 ml. Serum urea 32 mg. per 100 ml. Urine: nothing abnormal.

Light sensitivity tests on normal skin reveal no abnormal reaction.

Histopathology.—Throughout the cutis and in the adjoining subcutis there are large, well-defined islands of epithelioid cells with an admixture of lymphocytes, mostly at the margins of the nodules. A number of giant cells are present. The nodules are surrounded by scanty strands of connective tissue. There are also a few perivascular collections almost entirely lymphocytes. No caseation present. The reticulum stain shows a fine network of reticulum fibres which surrounds and permeates the infiltrate. The capillaries, especially in the upper corium, are widely dilated. Acid-alcohol fast bacilli have not been seen.

Comment.—Boeck described three clinical forms of cutaneous sarcoid to which later authors have added a number of variants. Boeck's sarcoid comprises (1) the small-nodular disseminated form: (2) the large-nodular localized and (3) the diffuse infiltrating form which is identical with Besnier's lupus pernio. Of these the first variety seems to be the least frequent. This form is distinct from the others by its often eruptive onset and its tendency to spontaneous remission or resolution (Kissmeyer, 1932: Pautrier, 1940). In the present patient this exanthematic form is combined with diffuse infiltrating lesions on the nose and cheeks.

A remarkable feature of this case is the strict localization to the light-exposed and obviously sunburned areas. The patient states that she has always been sensitive

to sunlight, that the first crops developed after intensive and prolonged sun-exposure and that an exacerbation ensued in the spring and summer. These facts suggest an actinic aetiological factor which as far as I could ascertain has not been reported so far. This localization is all the more difficult to explain as light treatment is a recognized therapy in sarcoid and has been applied in numerous cases.

In an attempt to explain this unusual occurrence I should like to recall the theory which has found the support of many observers, that the sarcoid lesion is an allergic

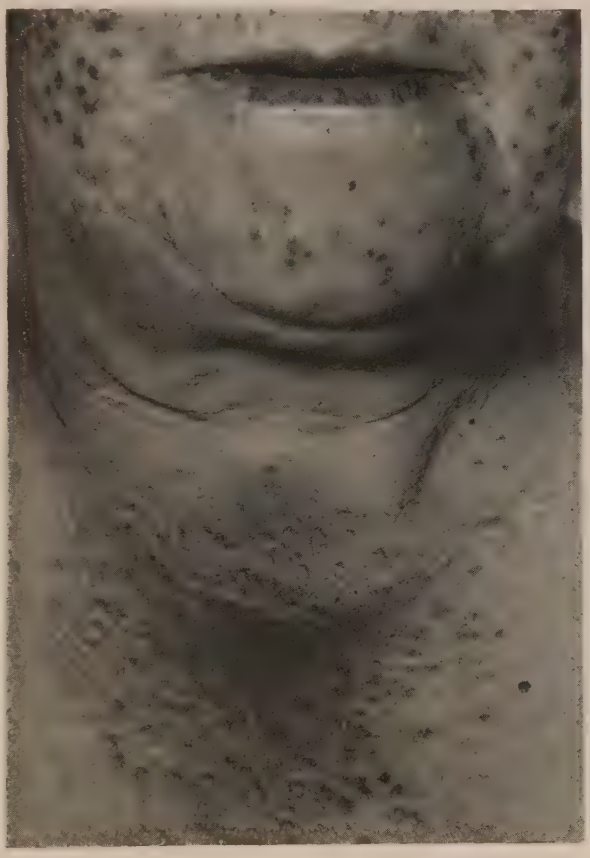

Fig. 1.—Disseminated small nodular sarcoid localized in face and *V* of the neck.

type of tissue reaction. The special reactibility of this patient may be caused either by photosensitivity or by the trauma produced in the skin by long and repeated sunburn. As the light sensitivity tests did not show any evidence of increased photo-sensitivity compared with a control person, the second assumption is the more acceptable. A number of cases have been reported where trauma seemed to have been the predisposing factor. Vosbein and Bonnevie (1940) recorded in their material of 37 cases two in which sarcoid lesions developed in old scars. In another of their patients lesions were localized in excoriations. Leitner (1942) reported a case where the first sarcoid lesion arose on a pustular lesion.

Richter (1941), by injecting Chinese ink into the normal skin of sarcoid patients, produced typical sarcoid lesions.

In our case possibly the damage caused to the skin by a severe sunburn was a stimulus for the outbreak of the cutaneous eruption in a patient suffering already from sarcoidosis of the lungs.

Although extensive involvement of the lungs has led to impairment of the pulmonary circulation and subsequent dilatation of the heart, there is no clinical evidence of other visceral organs being affected, and there is no enlargement of the superficial lymph glands which Schaumann stated to be invariably involved. As Schaumann demonstrated sarcoid changes in scarcely palpable lymph nodes and in the marrow of bones which were radiologically normal, the purely clinical evidence seems to be inconclusive.

I am indebted to Dr. R. T. Brain for his permission to publish the case.

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The following cases have been published in *Proc. R. Soc. Med.*, **47**, 1063 :

Pyogenic Granuloma. Multiple Local Recurrence Following Excision.—Dr. Clifford Evans.

? Reticulosis.—Dr. J. S. Pegum.

Sarcoidosis with Involvement of the Central Nervous System.—Dr. R. G. Howell for Dr. G. B. Mitchell Heggs.

The following cases also were shown :

Lichen Planus Annularis Atrophicus.—Dr. R. T. Brain.

(1) Cicatrizing Rodent Ulcer. (2) Sarcoidosis, with Lichenoid Lesions.—Dr. Brian Russell.

(1) ? Mast-cell Reticulosis. (2) Purpuric Drug Eruption due to Sedormid. Dr. M. Feiwel.

(1) Chronic Ulcerative Pyoderma. (2) Case for Diagnosis. ? Granuloma Annulare.—Dr. P. D. Samman.

THE NORTH OF ENGLAND DERMATOLOGICAL SOCIETY

Liverpool. 12 October 1954.

? Lymphocytoma.—Dr. J. H. S. Pettit (for Dr. D. G. Freshwater).

A girl aged 13.

Early in 1953 a well-demarcated eruption appeared on the forehead and nose. There have never been any symptoms.

The eruption consists of a band of small translucent papules spreading, just to the right of the midline, from the hair margin to the nose, where the papules also spread over the midline. A number of the lesions have a dilated plugged follicle in the centre of the papule.

Histology (Dr. Henry Haber).—The epidermis shows hyperkeratosis extending down into the follicles. The cutis shows perivascular and periappendicular infiltration of lymphoid cells which in some places invade the epidermis. The histology suggests lupus erythematosus. A further possibility is lymphocytoma.

Progress.—Treatment with mepacrine and chloroquine had no effect on the eruption.

OBITUARY

HENRI GOUGEROT.

(1881–1955)

CAT.

Henri Gougerot died on 15 January 1955. In him French dermatology has lost its undisputed leader and world dermatology one of its most illustrious figures.

His prodigious industry is indicated by the 2500 publications which have appeared under his name –dealing with rare and interesting cases, descriptions of new diseases and of new conceptions in the clinical and pathological fields. It is sufficient only to recall his description of sporotrichosis in 1906, his thesis on tuberculosis of 1907, the hypodermites in 1914, superficial microbial infections, capillaritis, nodular allergides, benign familial pemphigus and the *trisymptome* which bears his name. His books on dermatology, the treatment of syphilis and industrial dermatoses have gone through many editions. Gougerot saw everything and commented on everything which the present state of science allowed him to see, to foresee and to comment upon. His activities in the combat of venereal disease in France continued ardently and fruitfully since 1910. In the capacity of President or Secretary he was the activating spirit of many societies and official commissions in connection with venereal disease.

From 1928 to 1952 Gougerot was professor of the clinic of dermatology and syphilis at the Faculté de Médecine of Paris and of the St. Louis Hospital. He was a member of the *Académie nationale de Médecine* since 1940 and commander of the Legion of Honour. But among all the honours which came to him the greatest without doubt was that he was a uniting force between all French dermatologists and that he became, in his own country, the final arbiter on all matters of dermatology and venereology. His reputation was world wide. Since 1936, he was Honorary Foreign Member of the British Association of Dermatology ; he belonged to every foreign society and academy of dermatology.

Gougerot had no enemies, only friends, for his spirit was noble, frank, warm-hearted, tolerant and impartial. His loss will be sadly felt not only in France but in England and in the whole world. But if he has left us, his spirit will remain for long and secure his place among the great ones of dermatology. A. T.

Dr. W. J. O'DONOVAN.

Dr. O'Donovan who died on 13 January 1955 was born at Tonbridge on 20 September 1886, the eldest of the six children of Patrick O'Donovan of Clonakilty, County Cork. He entered The London Hospital Medical College in 1905 and qualified in 1909. He held the post of Junior Assistant Director at the Institute of Pathology and was a Medical Registrar when the Great War broke out. In this war he became Chief Medical Officer to the Ministry of Munitions and received the O.B.E. for his services. At this time he carried out important work on problems of TNT poisoning and of industrial medicine as a whole.

Returning to The London Hospital after the war, he at first continued in general medicine and later branched off into dermatology, succeeding Dr. Sequeira in 1926 as Physician-in-Charge of the Skin Department. The treatment of syphilis was at that time the responsibility of the dermatologist, until in 1930 the London County Council set up the Whitechapel Clinic.

Dr. O'Donovan wrote two books. One, *Dermatological Neuroses* in 1927, was one of the earliest works to emphasize the importance of emotional factors in skin diseases. The other was a small work on diseases of the hair. He made important contributions on the control and prevention of occupational diseases of the skin, and especially cancers caused by tar and arsenic.

CAT.

Dr. O'Donovan's teaching methods were most entertaining as well as instructive, and he usually had a large following. A secretary sat beside him, making such notes as he dictated or she thought necessary to record, while the Chief sat facing the patient, finger tips opposed, and fired a stream of pertinent questions, until from a combination of this questionnaire and keen observation of the patient's lesions and general bearing, a firm diagnosis was established.

In 1933 he was President of the Dermatological Section of the British Medical Association meeting in Dublin, and from 1939 to 1941 he was President of the Section of Dermatology of the Royal Society of Medicine.

Dr. O'Donovan's medical activities occupied only a part of his very busy life. In 1931 he became Conservative Member of Parliament for the Mile End division of Stepney, but could not retain the seat at the general election in 1935. He was also unsuccessful in a second attempt to re-enter Parliament at West Fulham in 1950, in opposition to Dr. Edith Summerskill. He was Chairman of the Conservative and Unionist Graduates Association of the University of London at the time of his death, and was President of this body for a number of years. He was elected to the Standing Committee of the Convocation of London University in 1949.

He was a leading figure in the Roman Catholic Church, and was appointed lay head of Catholic Action before World War II. For many years he acted as Secretary to the Association of Roman Catholic Doctors, the Guild of St. Luke, St. Comas and St. Damien. For this and other work he received in 1951 from Pope Pius XI the honour of Knighthood of the Order of St. Gregory the Great.

His fellow dermatologists will never forget Dr. O'Donovan's wonderful gift of oratory—part of his Irish inheritance. He will be missed by all, for such a personality is irreplaceable.

B. R.

BOSTON
NOV 2 1964
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BOOK REVIEWS.

A Fourth Edition*.

This is a completely revised version of a work which has appeared at eight-yearly intervals since 1930. It represents thirty years' experience of the author and pertinent additions from outside sources. Those who have done much writing will sympathize with Dr. Andrews's statement that "creating a new book necessitates being absorbed in the work so that the usual companionship of wife and children is mutually missed. Through their unselfish co-operation and forbearance they are in a sense co-authors".

The writing of prescriptions in English in accordance with the recent ruling of the Committee of Revision of the United States Pharmacopoeia runs contrary to the decision to revert to Latin in the new British National Formulary: surely a deviation between Anglo-American medical policy as significant as the adoption in sporting circles of different sizes of golf balls. The author himself regrets this change "since the therapeutic value of remedies for the numerous skin diseases in which the psyche plays a rôle may thus be lost". He does not mention that Latin still has its uses as a universal tongue.

This work has always been a pleasure to read. It is the *Times*, or even the *Manchester Guardian*, of dermatological reading, gently but firmly authoritative and with unobtrusive headlines. The references are neatly filed at the rear of each section and do not spread untidily at the foot of individual pages. The monochromatic illustrations are excellent and there has been no attempt at intermittent chromatic stimulation of the readers' interest. Photographs of special merit from other publications have also been included, with due acknowledgment.

Having said this, the reviewer can either look for mis-spellings hidden in the text or cross swords over aetiological concepts and therapeutic régimes. It would be courting disaster to challenge Dr. Andrews in the arena of fact.

It is a relief to see the circinate and gyrate dermatoses of Darier, Jadassohn, Lipschutz, Strempel and Wende designated simply as erythema annulare centrifugum.

A pleasing little section is that on p. 141, entitled "Eczema due to Anxiety". It is clear that the phenomenon of relapse after successful in-patient treatment as soon as the patient is told he may go home is not peculiar to this country.

What has Besnier done to deserve oblivion? We read of atopic dermatitis, with six synonyms, but his name is omitted, whereas Duhring's memory is perpetuated under "dermatitis herpetiformis". In connection with the treatment of this disorder, Promacetin is recommended in a dose of 0·5 g. twice a day. An hour of research revealed that this is an acetosulphone, available not in this country, but only in America. This example is typical of the difficulties of understanding treatments based in part on proprietary products. For example, what are Aveeno, Creal, Escobarb, Kivell, Linnet, Mazon, Polysporin, Tarstill, and Varidase? Some of these savour almost of "New-Speak".

The author describes Norwegian scabies as "encountered among lepers, among those suffering from wasting disease, and others living under insanitary conditions".

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* *Diseases of the Skin.* (4th Edition.). By George Clinton Andrews, M.D., F.A.C.P. (1954). Philadelphia: W. B. Saunders. Pp. 887. Illus. 777. Price £3 5*s*.

Surely the true basis is anaesthesia or hypo-aesthesia from whatever cause—leprosy, senile dementia, or mongolism.

For lupus vulgaris the author recommends isonicotinic acid hydrazide in an average dose for adults of 200 mg. to 300 mg. a day. Experience in this country suggests that 200 mg. is inadequate and 400 mg. usually gives a better result than 300 mg.

In the section on psoriasis it is disappointing to see no mention of the treatment of the patient as a whole with respect to maladjustments, yet three pages of directions are given on empirical, local and systemic remedies. The statement on p. 175 that the cause of this disease is unknown cannot be refuted, but precipitating and aggravating factors are given insufficient attention.

In the section on caverno-capillary haemangiomata three pages describe radiation therapy, surgery and injection procedures. A child's hand is illustrated before and after treatment with radium (1600 roentgen units) and it is stated : " No retardation of growth or other injurious changes are discernible three years later". One can only hope that this lack of sequelae will continue. Many dermatologists would not agree that spontaneous involution of caverno-capillary haemangiomata occurs only as a result of trauma, haemorrhage or infection, but is usually incomplete and accompanied by more scar formation than would result from proper (*sic*) therapy.

It is a pleasure to see acrodermatitis continua and otitis externa attributed firmly (*inter alia*) to *Pseudomonas aeruginosa*.

For a reviewer writing in the dyke-filling month of February it is a tonic to know that rest in the sunshine of Florida, Texas, Arizona or Southern California usually clears up the exudative discoid and lichenoid dermatitis of Sulzberger and Garbe.

Intravenous procaine hydrochloride given by an anaesthetist seems an unusual treatment for chronic urticaria. In spite of dryness of the mouth, metallic taste, dilatation of the pupils and effusion of tears, it is said to give a comfortable feeling of relaxation and sometimes of light-headedness.

This work is a trustworthy, balanced and well produced summary of present-day knowledge of dermatology. B. R.

Disturbances of Sweating.*

The writers of this book are acknowledged experts in their subject, having had extensive experience both in the field and in the laboratory, and the high expectations which such authorship raises are fully justified. The subject matter is divided into three sections The first deals with methods and results of investigative procedures in a manner which is sufficiently critical without being nihilistic. The second and longest section concerns the clinical aspect of the problem, which, for ease of description, is divided into hyperidrosis, hypoidrosis and dysidrosis ; and the various often closely inter-related syndromes are admirably described. The last section, devoted to therapy, while comprehensive and obviously largely based on personal experience, is disappointing in that it clearly shows how inadequate are the present methods of dealing with these manifold and common conditions.

The authors, as is only right, are enthusiasts and it may be that some readers will consider that undue importance is given to poral closure in a variety of otherwise unrelated dermatoses. Nevertheless, these views, based on reasoned and reasonable argument, are pleasantly provocative and further add to the value of the book.

The paper, print and photographs maintain the general high standard and an extensive bibliography, together with a subject and author index, also make this a useful book for reference. P. B.

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* *The Clinical Significance of Disturbances in the Delivery of Sweat.* By M. B. Sulzberger and F. Herrmann (1955). Springfield, Illinois : Chas. C. Thomas. Pp. 212. Figs. 55. Price 50*s*.

Histopathology of the Skin.*

Since the appearance of the first edition of Lever's very well known book many advances have been made in the field of histopathology of the skin. Civatte's work on bullous eruptions has now been widely accepted ; Masson's concept of cellular naevi is at last receiving world-wide recognition ; and the periodic acid Schiff stain has become a valuable help for the detection of fungi in tissues. These are but a few of the important advances made in the last five years. Several other less important contributions had to be considered and the author has incorporated all these in his new edition.

Fifty-six new photomicrographs have been added, and fourteen of the old ones replaced by better ones. There are twenty-one chapters, the first five dealing with the technique of biopsy, limitations of histological diagnosis, embryology, anatomy of the skin, laboratory methods and the morphology of mesodermal cells. The others cover the whole subject of dermatology, but curiously enough the author has omitted Molluscum sebaceum.

This book has been written by an expert for both the dermatologist and the general pathologist. It gives facts in a concentrated manner, and the brevity and exactness of the text is enhanced by an excellent revised bibliography which follows each chapter.

The print and paper are a credit to the publisher and all the photomicrographs are excellent. In spite of its heavy cost this book is recommended to every dermatologist interested in histopathology of the skin. To the general pathologist, to whom dermatologists turn more and more for advice and help, it will prove invaluable.

H. H.

Endogenous Eczema.†

This monograph deals with the disorder perhaps better known now as atopic dermatitis, Besnier's prurigo or disseminated neurodermatitis. The label endogenous would appear justified by the inability to find the main cause of the disease outside the individual.

In the introductory clinical chapter mention is made that infantile eczema represents both endogenous eczema and seborrhoeic eczema ; that in childhood the pattern tends to be particularly flexural in distribution ; that it often has a prurigo morphology ; that secondary bacterial infection imparts a polycyclic appearance ; that vitiligo-like pigmentary disturbances are not uncommon and that the outer part of the eyebrow is often lost—not entirely the result of rubbing (Hertoghe's sign). Lichen simplex chronicus, even when disseminated, is a different disorder. Isolated plaques on the dorsa of the hands cannot on morphological grounds be distinguished from eczemas of different aetiology. A graph of incidence shows a peak in the winter. The occurrence of asthma, vasomotor rhinitis, other eczemas, urticaria, diarrhoea, constipation and migraine in individual cases is statistically expressed.

The author then passes to his objective—to determine the pathological " constitution " found in the disorder. Eosinophilia, leucopenia, and abnormalities of plasma proteins are discussed, but what he is really after is to demonstrate abnormality in small blood vessels and in the autonomic nervous system generally. He shows the blood pressure to be unduly labile, the vasoconstrictor reaction to cold to be prolonged, and the arrectores pilorum muscles to act sluggishly ; sweat responses are changed

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*_Histopathology of the Skin_. By Walter F. Lever. Second Edition. 281 illustrations with 8 in colour. London : J. B. Lippincott Company. Price £4 16_s_.

†_Zur Pathogenese des Endogenen Ekzems_. By Doz. Dr. G. Korting. (1954) Stuttgart : G. Thieme Verlag. Pp. 107. Illus. 23. Price DM.13.80.

in the direction of hypoidrosis generally but hyperidrosis in the flexures, the usual seat of the disease. Water excretion tests were made, including tests following the injection of posterior pituitary extract and following irradiation of the mid-brain by short waves. The conclusion is reached that there is an abnormality in the hypothalamus leading to faulty regulation of the autonomic nervous system and that this is the pathogenic basis of the genetic disorder endogenous eczema and the related asthma and hay-fever.

The author may be quite correct in all he says, but the material is not presented in such a form as to give the feeling that the experiments have been well controlled. He moves too quickly and gives the impression of having decided on the facts in advance.

Difficulties of language apart, then, the practising English dermatologist will not find this book very useful. It should find a place however on the shelves of libraries of institutions where dermatological research is taking place.

M. F.

CORRESPONDENCE

The Editor, 'The British Journal of Dermatology.'

Sir,—Although I was the perpetrator of the persiflage referred to by Dr. J. H. Twiston Davies in his letter (1954, **66**, 458), may I say that I do not disagree with him. I merely supported mepacrine as the undoubted cause of tropical lichenoid dermatosis. Most of us will have seen identical lesions following gold therapy for rheumatoid arthritis, and I have no doubt that other drugs may produce these lesions. Therefore, with your permission, Sir, I beg to offer a few lines in honour of my old sparring partner.

O Twiston D. it's good to see
That phenobarb awakens thee
When most men's sleep is almost nil
Through taking much of good Guy's pill.
Though mepacrine has not your favour
Pray leave to us our only saviour,
Pheno !

I am, Sir,
Yours, etc.,
Allan Bigham.

Bradford,
January, 1955.

CURRENT LITERATURE.

THE CHILD WITH THE ITCHING SKIN. Vera B. Walker. (1954) *Acta allergol.*, **7**, 415.

Electrophoresis of histamine was used to treat infantile eczema, the dose being 2 c.c. of 1% solution at 1 milliamp. for approximately 10 minutes. Forty children were treated but shortage of space prevented detailed publication of results. Six cases are described in which it worked like a charm. H. T. H. W.

SKIN ALLERGY TO SIMPLE GASEOUS SULPHUR COMPOUNDS. V. Pirila. (1954) *Acta allergol.*, **7**, 397.

One case of urticaria due to sulphur dioxide and one of dermatitis due to hydrogen sulphide are reported. Exposure tests gave positive results in both. The sensitizing powers of various sulphur compounds are considered and the hazards of air pollution discussed.

H. T. H. W.

STEVENS-JOHNSON SYNDROME AND GRANULOCYTOPENIA AFTER PHENYLBUTAZONE. S. J. Steel and J. L. Moffatt. (1954) *Brit. med. J.*, i, 795.

A report of a severe degree of sensitivity to phenylbutazone with the features of Stevens-Johnson syndrome and granulocytopenia. B. A. T.

SYSTEMIC ANTIBIOTICS IN CERTAIN DERMATOSES. (1954) *Brit. med. J.*, i, 856.

A short report on the trial conducted under the auspices of the Medical Research Council to evaluate the effect of the newer antibiotics when given systemically in certain skin conditions. Neither aureomycin, chloramphenicol nor oxytetracycline was useful in herpes simplex, plantar warts, lichen planus, pityriasis rosea, dermatitis herpetiformis, or discoid eczema.

B. A. T.

RADIOTHERAPY IN ITS RELATION TO DERMATOLOGY. B. W. Windeyer. (1954) *Brit. med. J.*, i, 945.

In this Malcolm Morris Memorial Lecture the field of radiotherapy in dermatology is concisely covered. Also discussed are the action of radiation in dermatology, carcinogenesis, discrimination in the use of radiotherapy and the relations existing between radiotherapist and dermatologist.

B. A. T.

THE NUMBER OF MELANOCYTES IN HUMAN EPIDERMIS. G. Szabo (1954) *Brit. med. J.*, i, 1016.

In human epidermis the population density of melanocytes is of the order of 1000 per mm. in the skin of the thigh and arms, but may be twice to four times as great in the skin of the face and forehead. There is nevertheless a wide range of variation between the corresponding areas in different individuals. It is suggested that regional differences in the frequency of occurrence of melanomas may be primarily due to differences in the population density of melanocytes.

B. A. T.

ANTIHISTAMINE THERAPY WITH SPECIAL REFERENCE TO SKIN DISORDERS. R. P. Warin. (1954) *Brit. med. J.*, i, 1066.

The antihistaminic drugs available in this country are listed and compared, and certain practical points in their administration mentioned. Ill-effects of the drugs are discussed. It seems possible that the only conditions of the skin benefited by antihistamines are those in which whealing is part of the eruption. B. A. T.

INFANTILE ECZEMA TREATED WITH ORAL CORTISONE. Bethel Solomons, junr. (1954) *Brit. med. J.*, i, 1190.

Fifteen patients with infantile eczema were treated with oral cortisone. In six no benefit was observed, in another six there was a moderately good response and in three there was a gratifying result without return of symptoms. B. A. T.

RODENT ULCERS: AN ANALYSIS OF 711 LESIONS TREATED BY RADIOTHERAPY. Ian Churchill-Davidson and Ethel Johnson. (1954) *Brit. med. J.*, 1465.

An analysis is made of 711 rodent ulcers treated by radiotherapy, 98·9% being treated by three x-ray techniques.

The cure rate for all lesions treated over three years ago is 95·7% and for all those treated over five years ago 92·6%. Cosmetic results, recurrences and radionecrosis are discussed.

B. A. T.

THE SIGNIFICANCE AND MANAGEMENT OF PSORIASIS. John T. Ingram. (1954) *Brit. med. J.*, ii, 823.

His Watson-Smith Lecture is an admirable survey of psoriasis, and its aetiology, treatment, prognosis and abandoned theories are discussed. The author believes that, with the measures at present at our disposal the life of the psoriatic patient could be largely transformed if facilities were made available for the proper use of those measures. B. A. T.

EXFOLIATIVE DERMATITIS AFTER ACETARSOL VAGINAL PESSARIES. Bernard J. Peck. (1954) *Brit. med. J.*, ii, 850.

A case of exfoliative dermatitis from acetarsol in vaginal pessaries is described. It is suggested that this was due to induced drug hypersensitivity to acetarsol absorbed per vaginam.

B. A. T.

SOME CURRENT PROBLEMS IN INDUSTRIAL DERMATITIS. F. Ray Bettley. (1954) *Brit. med. J.*, ii, 905.

Present day difficulties in dealing with industrial dermatitis are dealt with under two headings. In the mainly medical group, the problems encountered concern doubtful diagnosis, the friction element and eczema sequels. The second group is concerned with medico-legal considerations and deals with procedure under the National Insurance (Industrial Injuries) Act, 1946. Mention is made of the tendency for the workman to receive the benefit of the doubt. A summary is given on measures for preventing dermatitis. B. A. T.

NASAL CARRIAGE IN STAPHYLOCOCCAL SKIN INFECTIONS. L. G. Tulloch. (1954) *Brit. med. J.*, ii, 912.

A brief account is given of the relevant studies in staphylococcal carriage.

A report is made of an investigation establishing, by phage-typing, the identity of strains of staphylococci carried in the anterior nares and those isolated from infections of the skin.

The importance of adequate sterilization of the anterior nares when treating staphylococcal skin infections is stressed, and methods of doing this are suggested. B. A. T.

ACUTE DIFFUSE LUPUS ERYTHEMATOSUS. H. L. Matthews and M. J. Meynell. (1954) *Brit. med. J.*, ii, 1140.

An unusual example of acute diffuse lupus erythematosus is described in which pulmonary manifestations predominated. Stress is laid on the value of looking for " L.E." cells in unusual pneumonias. B. A. T.

CATTLE RINGWORM. A. J. Rook and W. Frain-Bell. (1954) *Brit. med. J.*, ii, 1198.

The epidemiology, mycology and incidence of cattle ringworm in man are dealt with. A series of 39 cases is analysed for age, seasonal incidence, the sites affected and the clinical picture. In addition to *T. discoides*, which is the usual pathogen, *T. mentagrophytes* was responsible for some cases. B. A. T.

TREATMENT OF RÖNTGENCARCINOMA BY HYPERVITAMINISING WITH AXEROPHTHOLEN. F. Fleck. (1954) *Derm. Wschr.*, **130**, 1244.

The similarity between precancerous changes in the skin and A-avitaminosis has been noted ; the low level of vitamin A in precancerous tissue and its complete absence in cancer cells. This prompted the author's attempt at substitution therapy with carotinoid substances.

The patients gained 2–3 kg. in weight the first month especially when thyroxin was given in addition to the vitamin (patients with Basedow's disease rarely suffer from cancer and carotinoid

substances have a parasympathetic effect). Thyroxin is necessary to convert carotin into vitamin A and also lessens the risks of side effects from the hypervitaminizing therapy. Clinical photographs show the very satisfactory response obtained in four patients. In a fifth patient with a lesion of the external ear the treatment failed. The substitution therapy recommended is 300,000 u. of vitamin A daily by injection with 0·1–0·6 g. of thyroxin daily. Side effects from toxic carotinosis were not observed in spite of the protracted therapy. M. S. S.

THE IMPORTANCE OF HYALURONIDASE IN ECZEMA. O. Braun-Falco. (1954) *Derm. Wschr.*, **130**, 1081.

It is doubtful if hyaluronidase occurs in normal skin, but increased hyaluronidase activity has been found in the presence of inflammatory or allergic skin processes, and it has been suggested that antihistamines act mainly by inhibiting the spreading factor of hyaluronidase. In the author's experiment with injected solutions of dye and hyaluronidase, spreading tests and diffusion potentials were no different in eczema subjects, normal controls and psoriatics. Spraying of sound skin or of eczema patches with hyaluronidase solution (a greasy base might irritate) did not cause irritation (it actually improved some eczema areas) nor latterly did careful massive subcutaneous infiltration with the solution. In guinea-pig experiments sensitivity reactions obtained with 2, 4-dinitrochlorbenzene were not heightened by the injection of hyaluronidase solution.

The author concludes that there is no evidence from his experiments that hyaluronidase is important in the pathogenesis of eczema. M. S. S.

CHEMISTRY OF THE HORNY LAYER. H. W. Spier, G. Pascher and C. G. Schirren. (1954) *Derm. Wschr.*, **130**, 1158.

The authors analyse the water soluble constituents of eluates from the surface horny layers of normal skin and record their findings. Of particular interest is the surprise finding of an anion deficit, e.g. eluate from 100 g. of scrapings gave 85 m. eq. of bases to only 60 m. eq. of acids, yet the pH of the surface skin lies between 4·5 and 6·5. Heating of the eluate causes turbidity and increases the pH, probably due to the thermoinstability of an as yet unknown medium strong acid with the dissociation constant of formic or acetoacetic acid. Evaporation is slow at room temperature but increases rapidly from 50°. The variability of the pH of surface skin is small and linked to the isoelectric point of " keratin ", i.e. in the pH range of minimal swelling of the horny layer. M. S. S.

SEVERE BULLOUS OCCUPATIONAL DERMATITIS FROM RUTA GRAVEOLENS. L. Szegö and Vl. Dolmay. (1954) *Derm. Wschr.*, **130**, 1180.

To develop phytophotodermatitis requires sunshine, moisture, and contact with the fresh leaves or pollen of the Ruta graveolens (from which Rutin is obtained). The dorsum of the hands, fingers and feet are the sites most often affected (and cheeks from the contaminated hands). A patch test of dried leaf powder or its alcoholic extract is negative. M. S. S.

THE EXCRETION OF HEPARIN IN THE URINE. H. G. Piper and G. Wiedemann. (1954) *Derm. Wschr.*, **130**, 851.

By titrating urine with a watery solution of toluidine blue (e.g. 0·5%) one can demonstrate qualitatively the presence of heparin (in large, moderate or small amounts), the first flocculation being taken as the end point: the metachromasia found when using a clear watery solution of heparin is not seen with urine. After 300 mg. of heparin by mouth there was no flocculation on testing the urine and the bleeding time was uninfluenced: heparin given intravenously was rapidly excreted in the urine and flocculation was no longer obtainable after 6 hours; the bleeding time corresponded: given intramuscularly increasing quantities were detected in the urine up to 5 hours after the injection but no longer after 13 hours; the bleeding time had returned to normal earlier. M. S. S.

EXPERIMENTAL-MORPHOLOGICAL INVESTIGATIONS INTO THE ACTION OF THE SEXUAL HORMONE. H. Hermann. (1954) *Derm. Wschr.*, **129**, 489.

In male guinea-pigs after an injection of proluton measurable changes were observed in the volume of cells or their nuclei (increase or shrinkage) in the anterior horns of the spinal cord, cerebral cortex, ganglia of the sympathetic chains, epithelium of the large and small bowel,

liver, islets of the pancreas, epithelium of the tubuli contorti and of the urinary canals in the kidneys. The dosage was not within a physiological range. M. S. S.

COMPARATIVE EFFECTS OF AMINOPTERIN CORTISONE AND A.C.T.H. IN EXPERIMENTAL FORMALDEHYDE ARTHRITIS AND PSORIATIC ARTHRITIS. R. Gubner, L. Cote, J. Hughes, J. J. Oleson, J. M. Ruegsegger and J. H. Williams. (1952) *J. invest. Derm.*, **19**, 297.

Cortisone A.C.T.H. aminopterin and salicylates are all very effective in reducing the damage done to the tarsus by injection of formalin into the plantar fascia of a rat. Aminopterin is specifically neutralized by pteroylglutaminic acid and the citrovorum factor neither of which interfere with cortisone or A.C.T.H. Oddly enough the action of A.C.T.H. was not very much impaired by castration or adrenalectomy : so perhaps all these things act directly on the connective tissues.

Aminopterin enhances the action of cortisone in arthritis so that less need be given. In psoriatic arthritis its effect on the psoriasis is greater than that of cortisone. The benefit in all cases is quite temporary. J. H. T. D.

ZIRCONIUM-PYRIBENZAMINE CREAM FOR THE PROPHYLAXIS OF RHUS DERMATITIS. R. E. Strauss and C. R. Bruck (1953). *J. invest. Derm.*, **20**, 411.

" Among Army personnel, poison ivy, oak and sumac dermatitis are a frequent occurrence since the soldiers inadvertently come into contact with the offending weeds in order to carry out their required field duty."

Of each of 3 groups of about 300 men who occupied in succession the same bivouac, one-third received an issue of the prophylactic cream, another third a facsimile dummy, a third no treatment at all. It does not say that the selection was random. The cream was applied only to face and hands, but we are not informed if the subjects were told what it was for, but since they were questioned about rhus dermatitis before the exposure they had a good opportunity to guess.

That a slightly higher percentage of those using the dummy than of the untreated controls became casualities supports the figures which show statistically significant results in favour of the cream. Another 100 men were treated with the cream about an hour after exposure, but since 40% of them developed dermatitis it could be assumed that the protection is not retrospective. J. H. T. D.

RELATIONSHIP OF THE SPREAD OF INDIAN INK TO THE HAIR CYCLE IN RABBIT SKIN. J. G. Strauss and A. M. Kligman. (1953) *J. invest. Derm.*, **20**, 425.

The hair of poodles, sheep and people resembles a population ; each hair lives out its span and falls. In some short-haired animals—guinea-pigs for example—and indeed in the eyebrows of the presenile a tidy effect is secured by the very short life of each hair. But in rats, mice and rabbits there is a hair growth cycle that travels like a wave over the coat, replacing the hair in such a manner that while in one part of the animal there are only *beet-haare* in another there are actively growing hairs.

Plucking automatically starts a fresh cycle. If therefore a shaved area shows no growth in 5 days it can be deemed to be in telophase, and since plucking in the neighbourhood will at once establish anaphase, comparable areas can thus be obtained side by side.

What difference the hair cycle may make to the spread of ink must be left to the reader to decide on the evidence supplied. J. H. T. D.

STUDY OF ELECTROPHORESIS IN 13 CASES OF PSORIASIS. M. Bolgert, J. Blamoutier and Mme. Moret. (1954) *Ann. Derm. Syph., Paris*, **81**, 616.

No characteristic electrophoretic variation was found in the blood in psoriasis. F. F. H.

KERATO-ACANTHOMA (MOLLUSCUM SEBACEUM). Ad. Dupont. (1954) *Ann. Derm. Syph., Paris*, **81**, 621.

The author described an instance of this condition in 1930. He now reviews the literature and adds 28 cases of his own with a useful account of the histology. He believes that the initial site of the lesion is in the infundibulum of the hair follicle. He has never seen one of these tumours disappear spontaneously, but, on the contrary, has observed malignant changes in six patients. F. F. H.

MUCOCUTANEOUS MANIFESTATIONS OF PERIARTERITIS NODOSA. Yves Bureau and Henri Barriere. (1954) *Ann. Derm. Syph., Paris*, **81**, 601.

The authors describe a man of 41 who, besides general symptoms, developed bullae, erythemato-squamous lesions and little red papules on the skin, and also painful purpuric spots on the fingers. The histology is described and the literature reviewed on the subject of the various types of cutaneous and mucosal eruptions. F. F. H.

THE CAPILLARY RESISTANCE IN ALLERGIC DISEASES. A. P. J. van der Burg. (1955) *Acta allergol.*, **8**, 1.

A method of estimating capillary resistance by negative pressure is described and the physiological differences in the permeability of the skin capillaries are discussed. The changes in capillary resistance after administration of histamine, antihistaminics, calcium, adrenaline, ACTH and cortisone in normal and allergic persons are reported. In allergic purpura intravenous injection of an antihistaminic is followed by an increase in capillary resistance. H. T. H. W.

OBSERVATIONS REGARDING THE URTICARIAL REACTION TO EGG WHITE IN INFANTILE ECZEMA. SCHULTZ-DALE EXPERIMENTS ON SENSITIZATION OF GUINEA-PIGS. R. Brun. (1955) *Acta allergol.*, **8**, 22.

Guinea-pigs sensitized to egg white are shown to be sensitive to the flesh of hens but not to that of ducks. H. T. H. W.

INVESTIGATIONS INTO THE EFFECT OF AUTO-HEMOTHERAPY. V. Aasted Frandsen and T. Samsoe-Jensen. (1955) *Acta allergol.*, **8**, 26.

Auto-haemotherapy was given to 16 patients with various skin diseases. Eosinophil counts and estimation of urine 17-ketosteroids showed no evidence of adrenocortical stimulation. H. T. H. W.

ON DERMATITIS CAUSED BY SYNTHETIC RESINS. V. Pirila. (1955) *Acta allergol.*, **8**, 62.

Of 130 workers in a sulphite cellulose factory 37 developed dermatitis. Most gave positive patch tests to phenol formaldehyde resins. The exposure period was usually 2–4 weeks, but reduced to 2–3 days in recurrences. Dermatitis may result from the raw materials as well as the products of condensation or polymerization of the resins. H. T. H. W.

THE GLOMUS TUMOUR. E. S. J. King. (1954) *Practitioner*, **173**, 687.

Glomus tumours are regarded as hamartomata of the glomus body. Glomera are arterio-venous shunts and those related to large vessels, e.g. carotid, jugular, vagal, aortic bodies, are *chemo-receptors* capable of influencing the blood flow over a wide area. Smaller bodies are found in the skin (especially on the extremities). They are stimulated by temperature changes and control the vascular supply of a more restricted area. Glomus tumours may arise from pre-existing glomus bodies, but possibly also from non-glomerular tissue. Distribution of tumours corresponds closely with that of normal bodies. The superficial tumours occur usually in subcutaneous tissues, more commonly on the upper extremity and often beneath the nail. The outstanding clinical feature is extreme tenderness accompanied by pain which is usually severe, continuous or paroxysmal, precipitated by touch, pressure or temperature change and frequently radiating over the whole limb. The pain is sometimes associated with flushing and sweating of the affected area. " Trophic " bone changes are also described. Occasionally with multiple tumours pain is absent, but a single painful nodule gives a diagnostic clue. Microscopically the tumour consists of numerous blood vessels surrounded by a zone of " glomus cells ", smooth muscle elements and numerous nerve fibres. Complete surgical removal usually cures. R. J. C.

LUPOID ROSACEA. G. Klingmuller. (1954) *Derm. Wschr.*, **130**, 1058.

The author described the clinical findings in two patients, one with lupoid rosacea, the other with lupus follicularis disseminatus faciei with no rosacea. A typical lupoid infiltrate was found histologically in both, but no tubercle bacilli ; nor was there other clinical evidence of tuberculosis. The former did not respond to vitamin D_2 or to isonicotinic acid hydrazide ; the latter responded rapidly. The author suggests that response to therapy may help to distinguish the two conditions. M. S. S.

THE RELATIONSHIP BETWEEN DERMATOMYOSITIS AND ADRENAL CORTEX. M. Müller. (1954) *Derm. Wschr.*, **130**, 1287.

Dermatomyositis is a chronic disease of unknown aetiology. Many of its manifestations can be explained on the basis of an insiduous adrenocortical insufficiency. But since this is only one factor in the causation, others mentioned being trauma, tumours and infection, replacement therapy cannot be expected to bring about more than the temporary alleviation of symptoms which is usually observed. W. G. T.

COMPARATIVE LABORATORY AND CLINICAL INVESTIGATION OF CERTAIN NEW FUNGICIDES AND DYES IN SUPERFICIAL DERMATOMYCOSES. J. Schönfeld. (1954) *Derm. Wschr.*, **130**, 1293.

The efficacy of a number of modern fungicides is compared with that of a number of dyes both *in vitro* and in patients. In a number of cases in which the more recent commercial preparation had failed solutions of dyes have been successful. The investigation included *Trichophyton interdigitale, gypseum, mentagrophytes* and *Candida albicans*. It is mentioned that both newer chemicals and dyes are ineffective in microsporon infection and favus. W. G. T.

ERYTHEMA ANNULARE CENTRIFUGUM (DARIER). S. Tappeiner. (1954) *Derm. Wschr.*, **130**, 1334.

A number of other erythematous dermatoses can easily be classified under the picture described by Darier as erythema annulare centrifugum. These are erythema gyratum perstans (Colcott Fox), which those who demand chronological accuracy may wish to have adopted as name for the group, erythema figuratum (Wende), erythema papulosum vel urticatum, figuratum, perstans et chronicum (Lustgarten), erythema exsudativum perstans (O. Sachs), erythema marginatum perstans (Finny), erythema gyratum perstans (R. Jaffe), and erythema rheumaticum marginatum (Keil). Differential diagnosis is mainly from dermatitis herpetiformis, urticarial eruptions, mycosis fungoides, syphilides and granuloma annulare. Various aetiological factors have been mentioned but the prompt action of penicillin suggests an infectious origin. W. G. T.

MYCOSIS FUNGOIDES, RESISTENT TO RADIATION, AND EOSINOPHILIC GRANULOMA. W. Gertler. (1954) *Derm. Wschr.*, **130**, 1220.

A number of cases of mycosis fungoides resistant to radiation therapy have been described. Examination of the literature of the past thirty years has not revealed any cases which could be diagnosed as eosinophilic granuloma. Two cases of mycosis fungoides affecting mainly the face and hardly responding to x-rays are described. There can be no doubt as to the identity of eosinophilic granuloma of the face, or of the eosinophilic granuloma of bone of children with occasional skin manifestation. There remains however a heterogenous group which Lever calls symptomatic eosinophilic granuloma of the skin. Great care should be taken in removing any cases from this latter group in the attempt to establish a new disease entity. W. G. T.

THE TREATMENT OF ALOPECIA WITH FRESH PITUITARY CELLS. H. Flegel. (1954) *Derm. Wschr.*, **130**, 1263.

The author comes to the conclusion that treatment of alopecia by intramuscular injection of suspensions of calf's pituitary in saline with the addition of penicillin is not superior to other forms of treatment and should be abandoned. W. G. T.

WOMAN'S CLOTHING, WOMAN'S OCCUPATION, WOMAN'S SKIN. R. Frühwald. (1954) *Derm. Wschr.*, **130**, 1266.

Under this fascinating title the author enumerates a multitude of dermatological hazards to which present day women are exposed in the course of their various activities. W. G. T.

THE SOCIAL SIGNIFICANCE OF COSMETIC TREATMENT. H. Ettl and R. Santler. (1954) *Derm. Wschr.*, **130**, 1367.

Because of the increasing number of patients seeking advice for cosmetic disabilities a special clinic was opened in the University Dermatological and Venereological Clinic at Vienna. Objections were raised on the grounds that this treatment did not constitute a medical necessity. A joint investigation with the neurological clinic clearly showed that the psychological repercussions of even minor cosmetic abnormalities justified treatment of these by the medical profession.

W. G. T.